FIG. 1

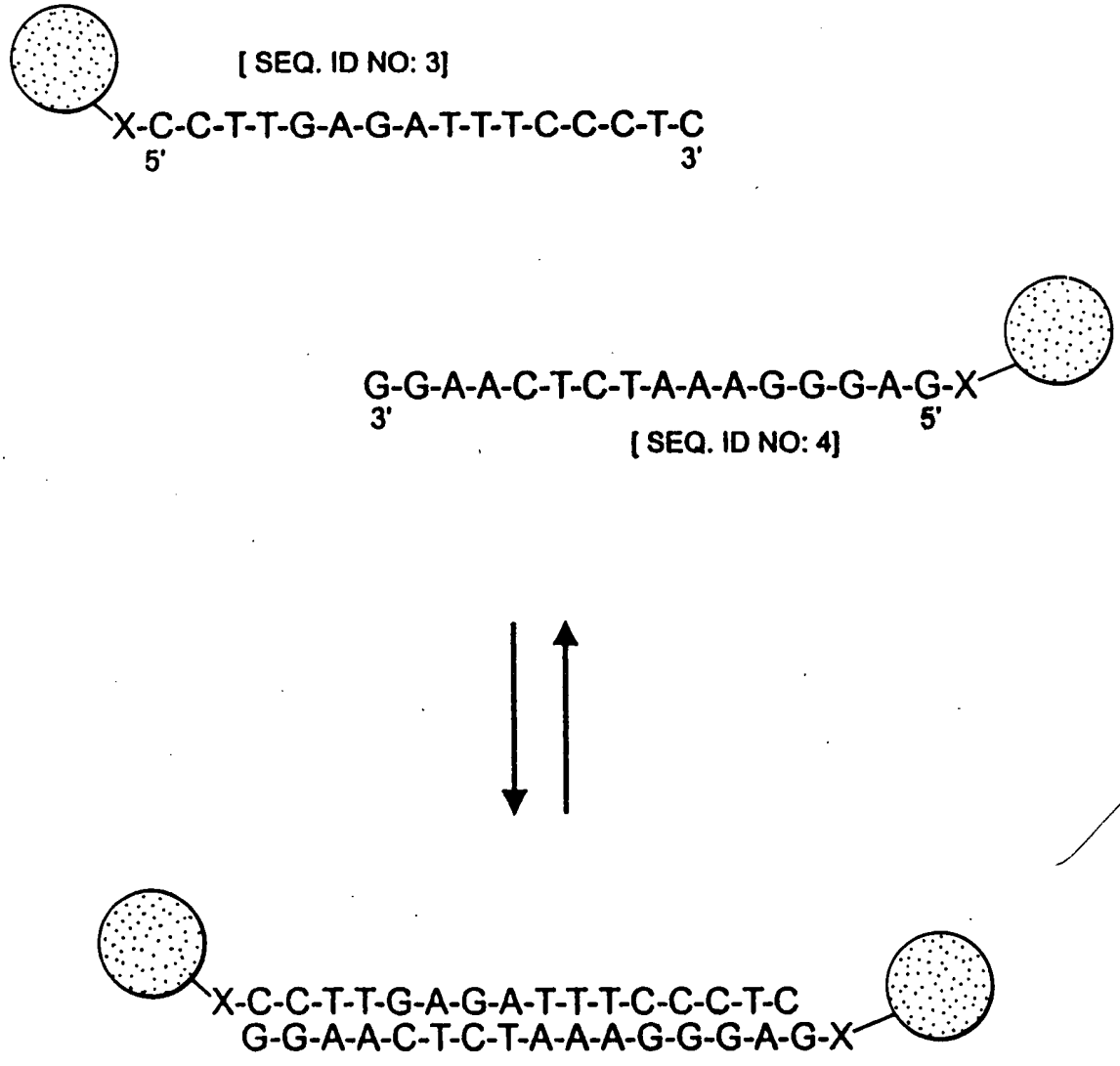

[SEQ. ID NO: 3]
X-C-C-T-T-G-A-G-A-T-T-T-C-C-C-T-C
5'
3'
G-G-A-A-C-T-C-T-A-A-A-G-G-G-A-G-X
3'
5'
[SEQ. ID NO: 4]
X-C-C-T-T-G-A-G-A-T-T-T-C-C-C-T-C
G-G-A-A-C-T-C-T-A-A-A-G-G-G-A-G-X

FIG. 2

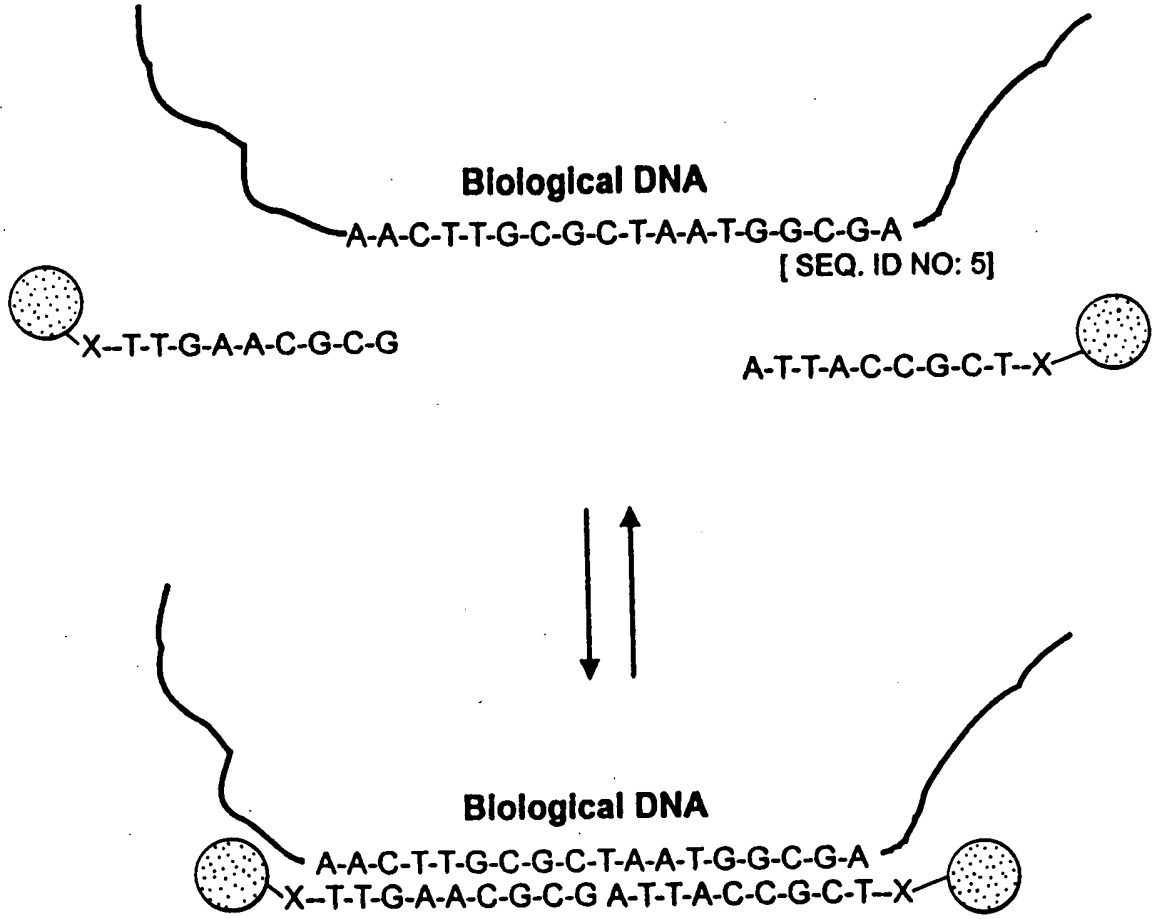

Biological DNA
A-A-C-T-T-G-C-G-C-T-A-A-T-G-G-C-G-A
[SEQ. ID NO: 5]
X--T-T-G-A-A-C-G-C-G
A-T-T-A-C-C-G-C-T--X
Biological DNA
A-A-C-T-T-G-C-G-C-T-A-A-T-G-G-C-G-A
X--T-T-G-A-A-C-G-C-G A-T-T-A-C-C-G-C-T--X

FIG. 3

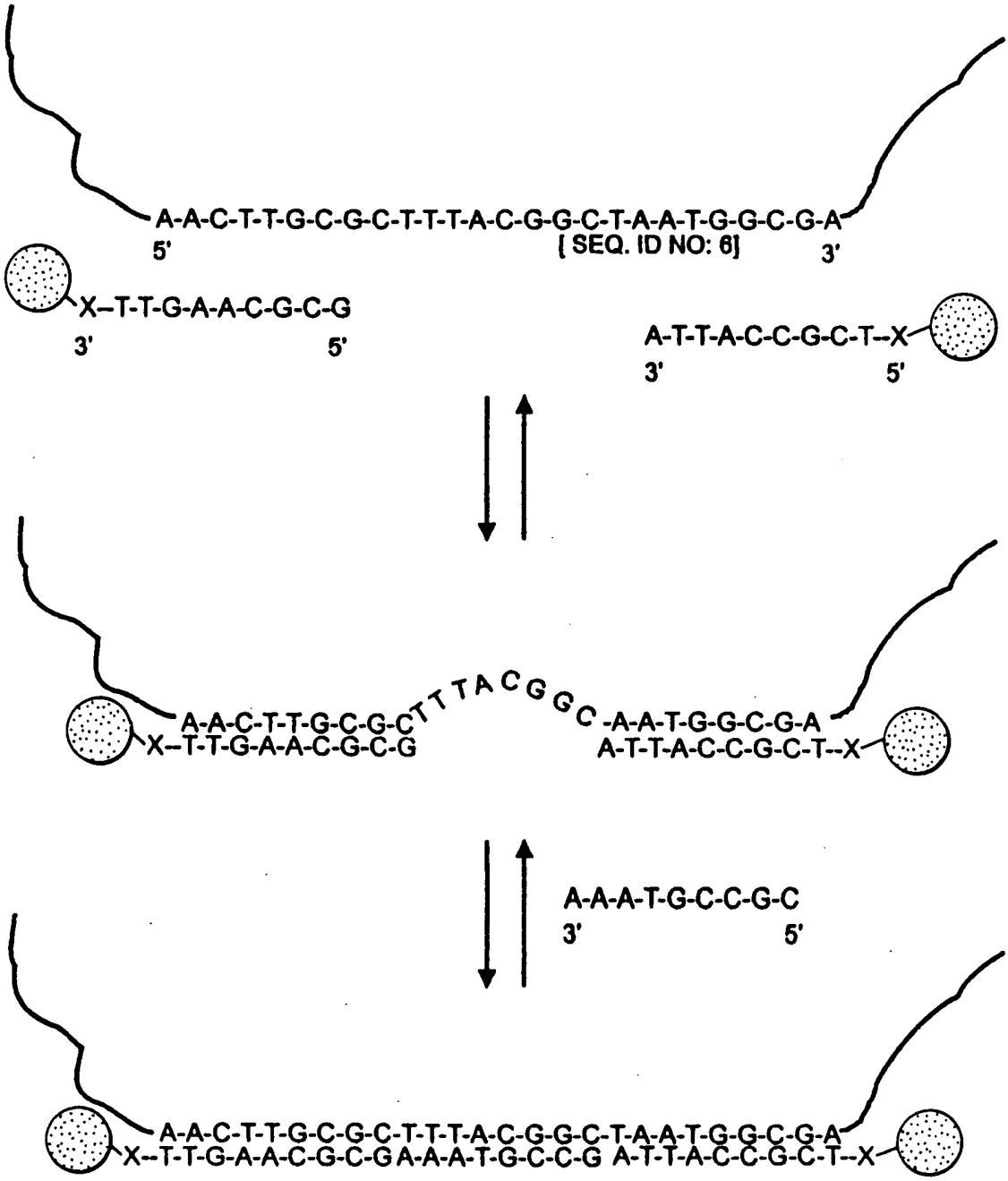

A-A-C-T-T-G-C-G-C-T-T-T-A-C-G-G-C-T-A-A-T-G-G-C-G-A
5'
[SEQ. ID NO: 6]
3'
X–T-T-G-A-A-C-G-C-G
3'
5'
A-T-T-A-C-C-G-C-T–X
3'
5'
A-A-C-T-T-G-C-G-C
T T T A C G G C
-A-A-T-G-G-C-G-A
X–T-T-G-A-A-C-G-C-G
A-T-T-A-C-C-G-C-T–X
A-A-A-T-G-C-C-G-C
3'
5'
A-A-C-T-T-G-C-G-C-T-T-T-A-C-G-G-C-T-A-A-T-G-G-C-G-A
X–T-T-G-A-A-C-G-C-G
A-A-A-T-G-C-C-G
A-T-T-A-C-C-G-C-T–X

FIG. 4

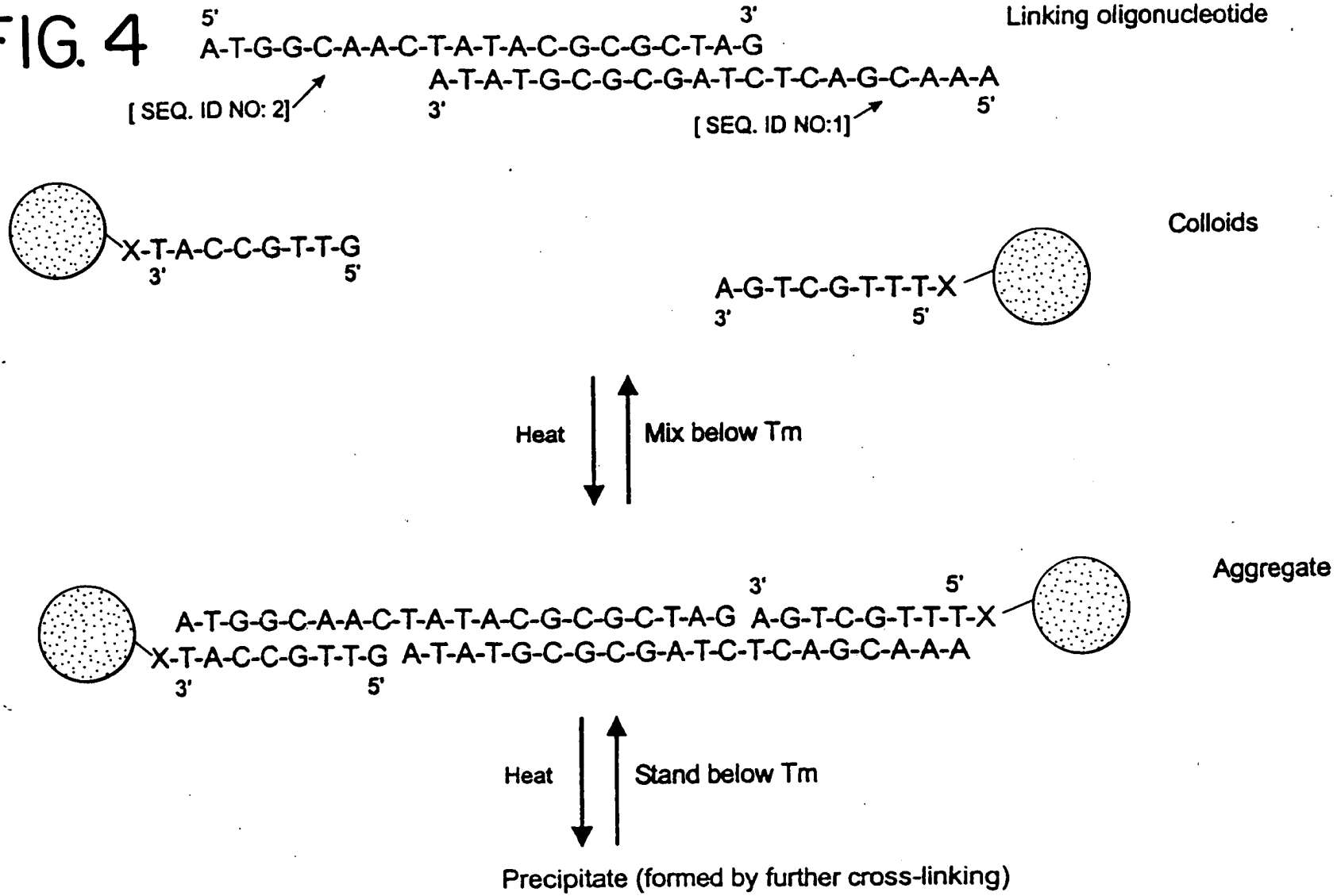

5'
3'
Linking oligonucleotide
A-T-G-G-C-A-A-C-T-A-T-A-C-G-C-G-C-T-A-G
A-T-A-T-G-C-G-C-G-A-T-C-T-C-A-G-C-A-A-A
[SEQ. ID NO: 2]
3'
5'
[SEQ. ID NO:1]
X-T-A-C-C-G-T-T-G
3'
5'
Colloids
A-G-T-C-G-T-T-T-X
3'
5'
Heat
Mix below Tm
4/64
Aggregate
3'
5'
A-T-G-G-C-A-A-C-T-A-T-A-C-G-C-G-C-T-A-G A-G-T-C-G-T-T-T-X
X-T-A-C-C-G-T-T-G A-T-A-T-G-C-G-C-G-A-T-C-T-C-A-G-C-A-A-A
3'
5'
Heat
Stand below Tm
Precipitate (formed by further cross-linking)

FIG. 5

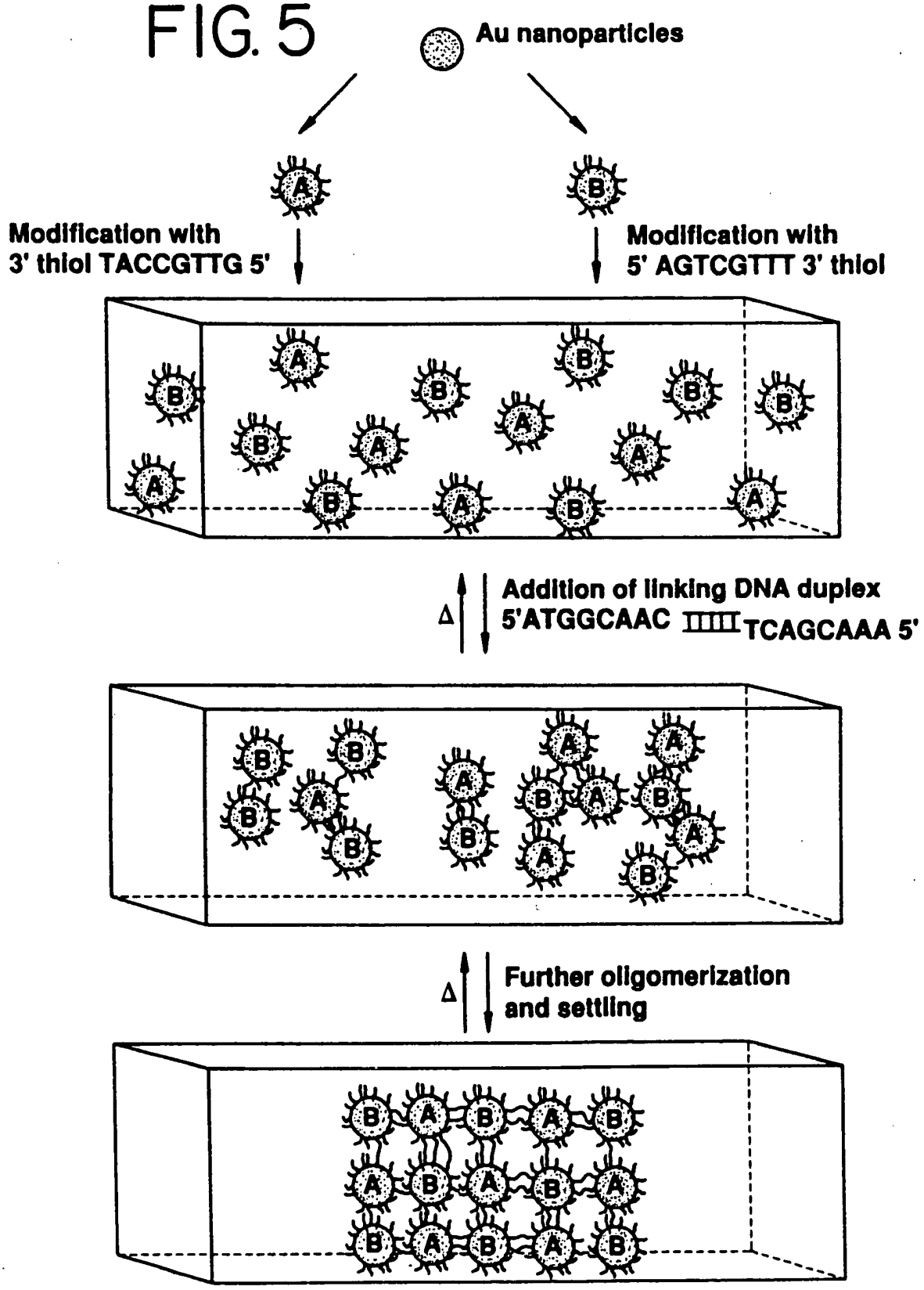

Au nanoparticles
A
B
Modification with
3' thiol TACCGTTG 5'
Modification with
5' AGTCGTTT 3' thiol
Δ
Addition of linking DNA duplex
5'ATGGCAAC IIIII TCAGCAAA 5'
Δ
Further oligomerization
and settling

FIG. 6A

FIG. 6B

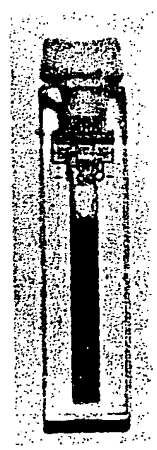


FIG. 6C

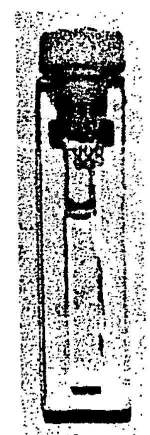


FIG. 7

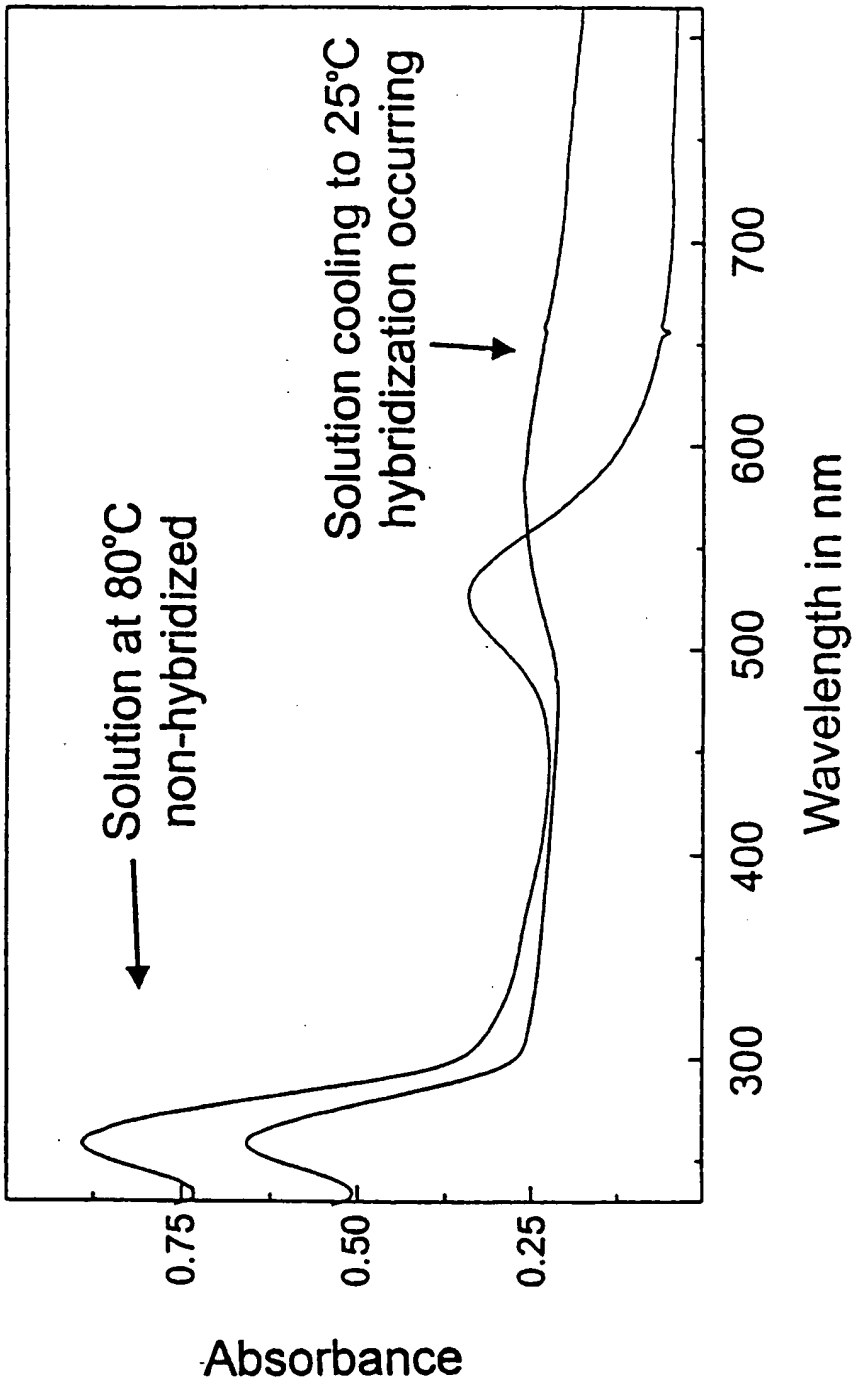

Solution at 80°C
non-hybridized
Solution cooling to 25°C
hybridization occurring
0.75
0.50
0.25
Absorbance
300
400
500
600
700
Wavelength in nm

FIG. 8A

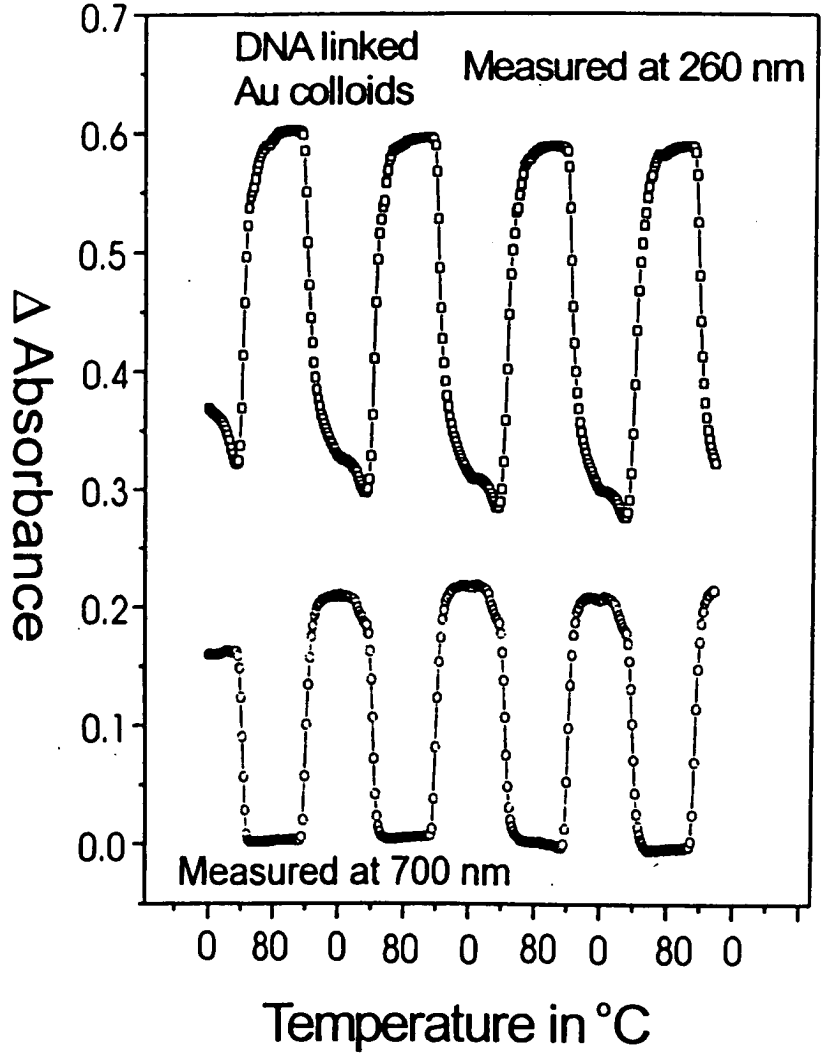

DNA linked
Au colloids
Measured at 260 nm
Measured at 700 nm
Δ Absorbance
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0
0 80 0 80 0 80 0 80 0
Temperature in °C

FIG. 8B

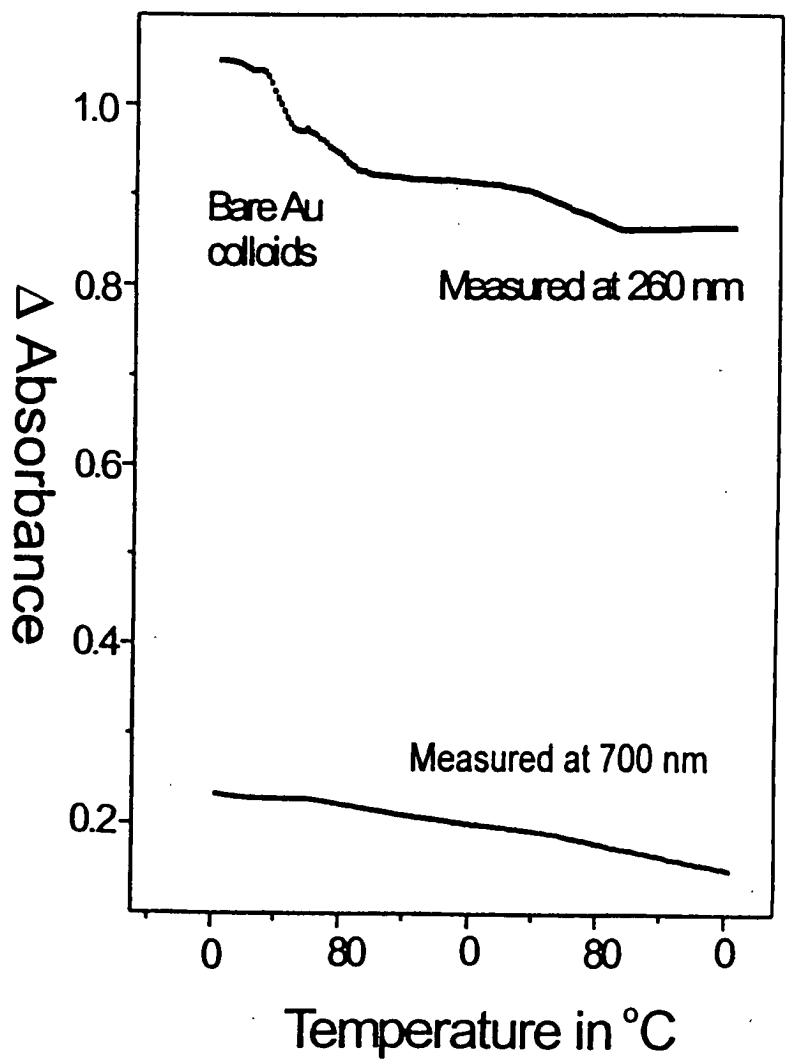

Bare Au
colloids
Measured at 260 nm
Measured at 700 nm
Δ Absorbance
1.0
0.8
0.6
0.4
0.2
0 80 0 80 0
Temperature in °C

FIG. 9A

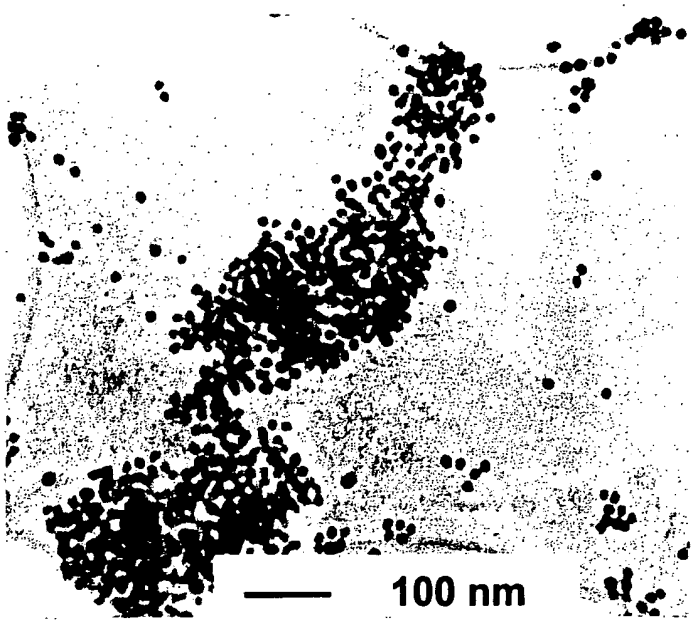


FIG. 9B

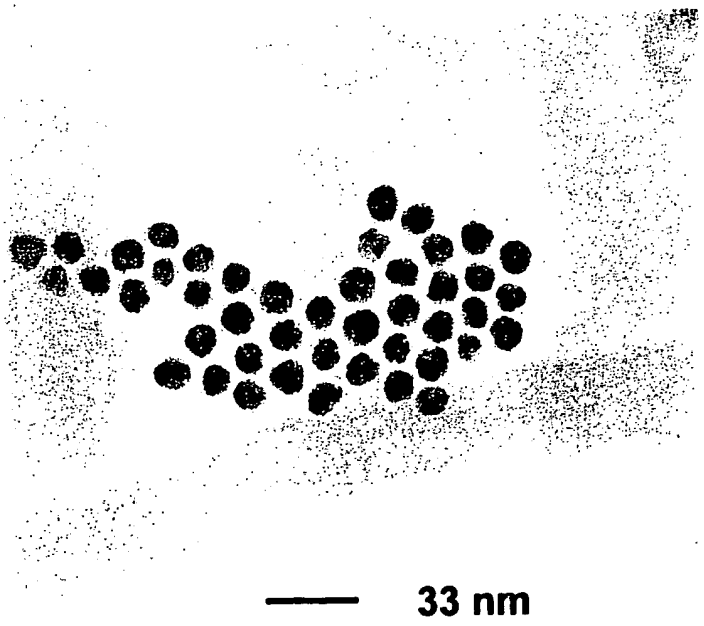


FIG. 10

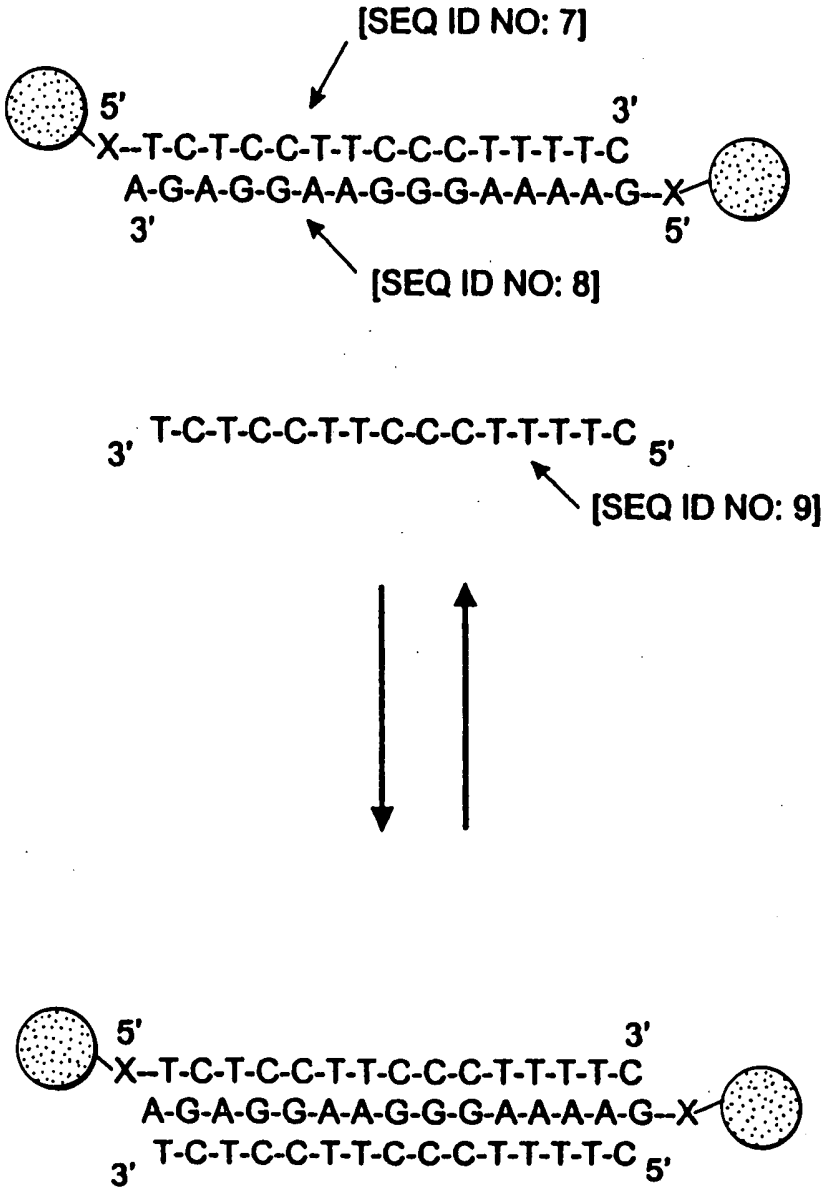

[SEQ ID NO: 7]
5'
3'
X--T-C-T-C-C-T-T-C-C-C-T-T-T-T-C
A-G-A-G-G-A-A-G-G-G-A-A-A-A-G--X
3'
5'
[SEQ ID NO: 8]
3' T-C-T-C-C-T-T-C-C-C-T-T-T-T-C 5'
[SEQ ID NO: 9]
5'
3'
X--T-C-T-C-C-T-T-C-C-C-T-T-T-T-C
A-G-A-G-G-A-A-G-G-G-A-A-A-A-G--X
3' T-C-T-C-C-T-T-C-C-C-T-T-T-T-C 5'

FIG. 11

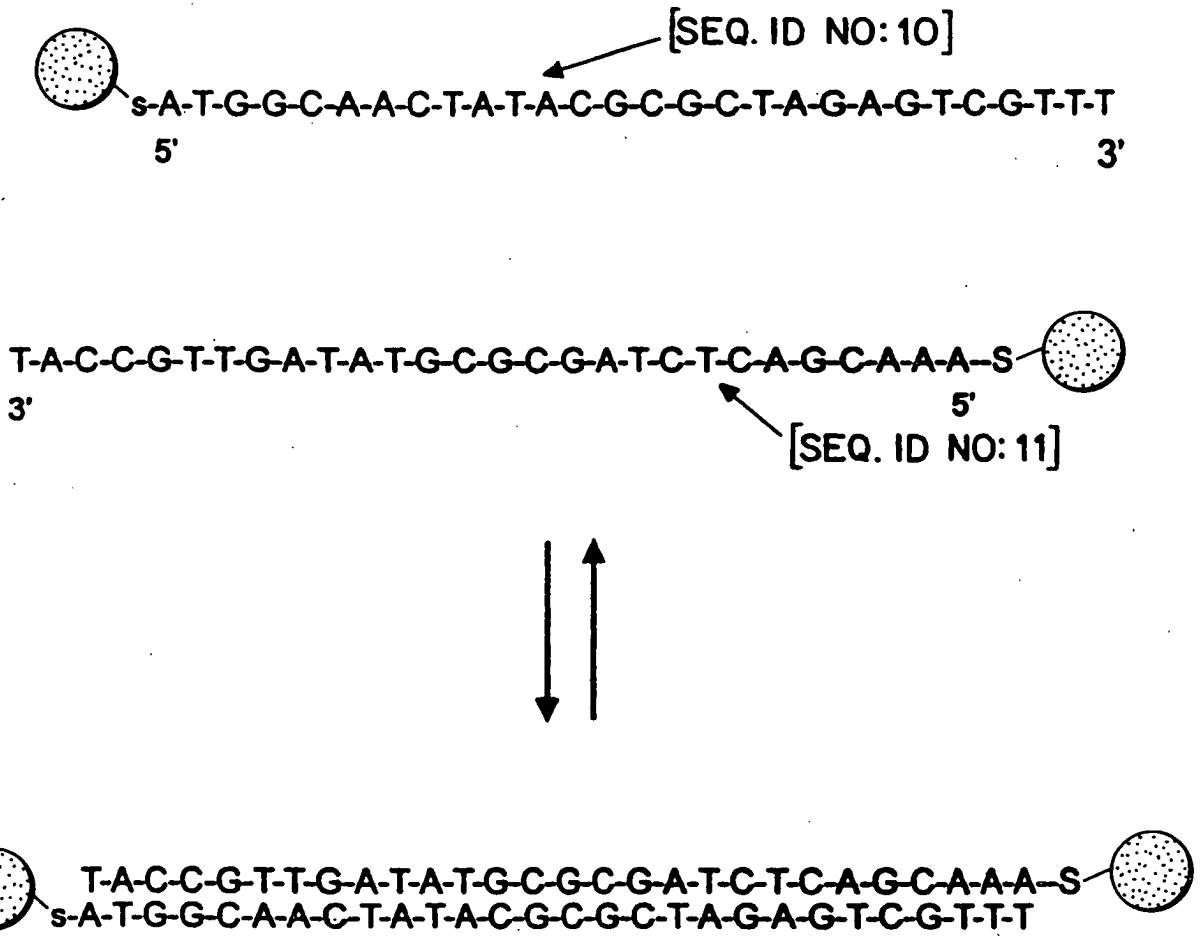

[SEQ. ID NO: 10]
s-A-T-G-G-C-A-A-C-T-A-T-A-C-G-C-G-C-T-A-G-A-G-T-C-G-T-T-T
5'
3'
T-A-C-C-G-T-T-G-A-T-A-T-G-C-G-C-G-A-T-C-T-C-A-G-C-A-A-A-S
3'
5'
[SEQ. ID NO: 11]
T-A-C-C-G-T-T-G-A-T-A-T-G-C-G-C-G-A-T-C-T-C-A-G-C-A-A-A-S
s-A-T-G-G-C-A-A-C-T-A-T-A-C-G-C-G-C-T-A-G-A-G-T-C-G-T-T-T

FIG. 12A

Complementary Target

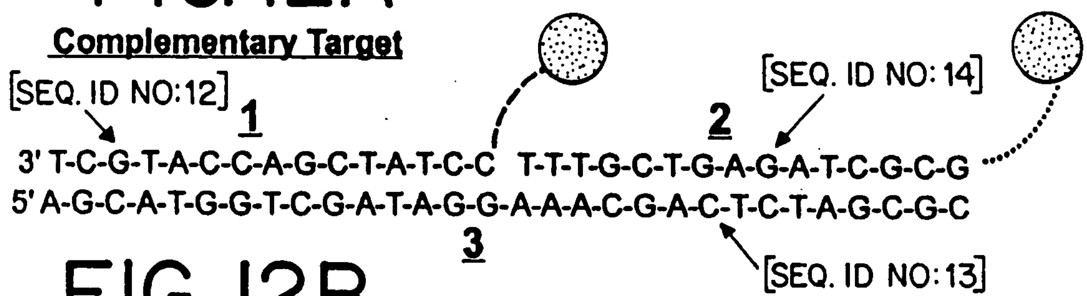


FIG. 12B

Probes without Target

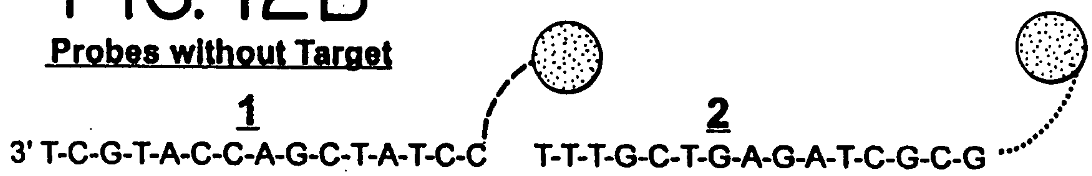


FIG. 12C

Half Complementary Target

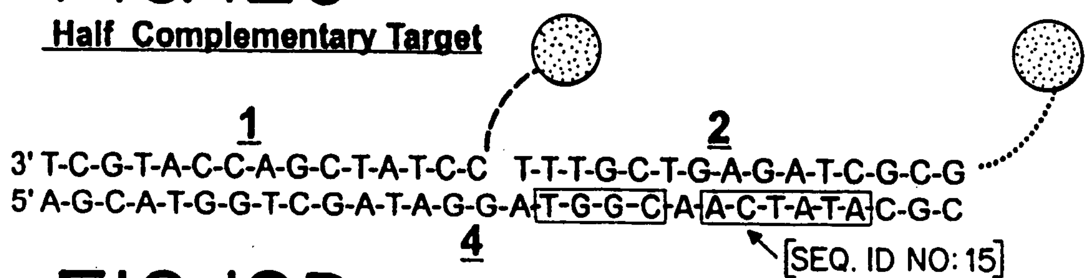


FIG. 12D

Target - 6 bp

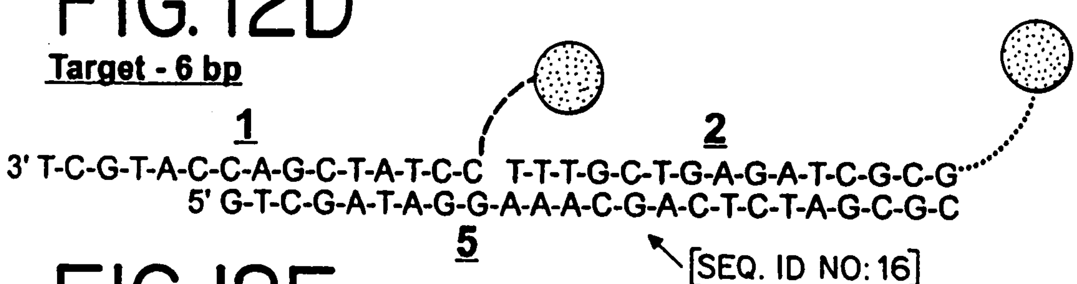


FIG. 12E

One bp Mismatch

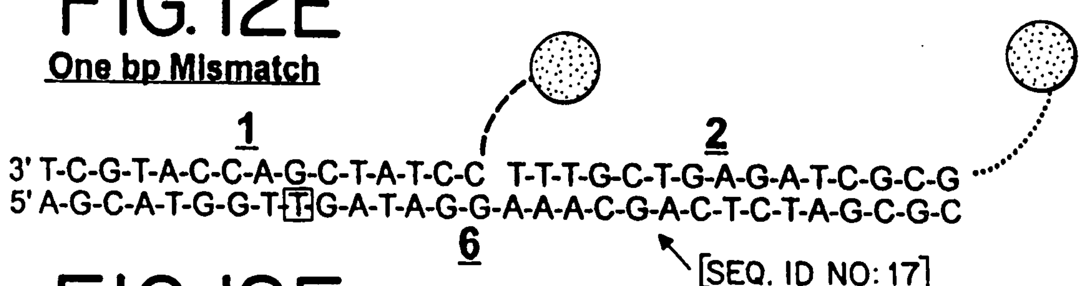


FIG. 12F

Two bp Mismatch

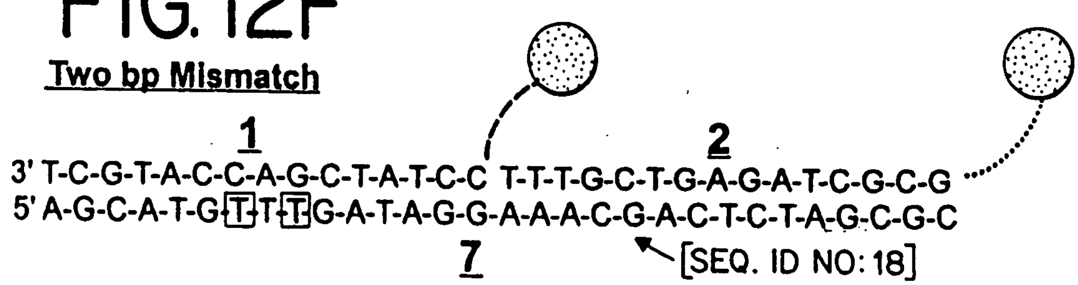


FIG. 13A

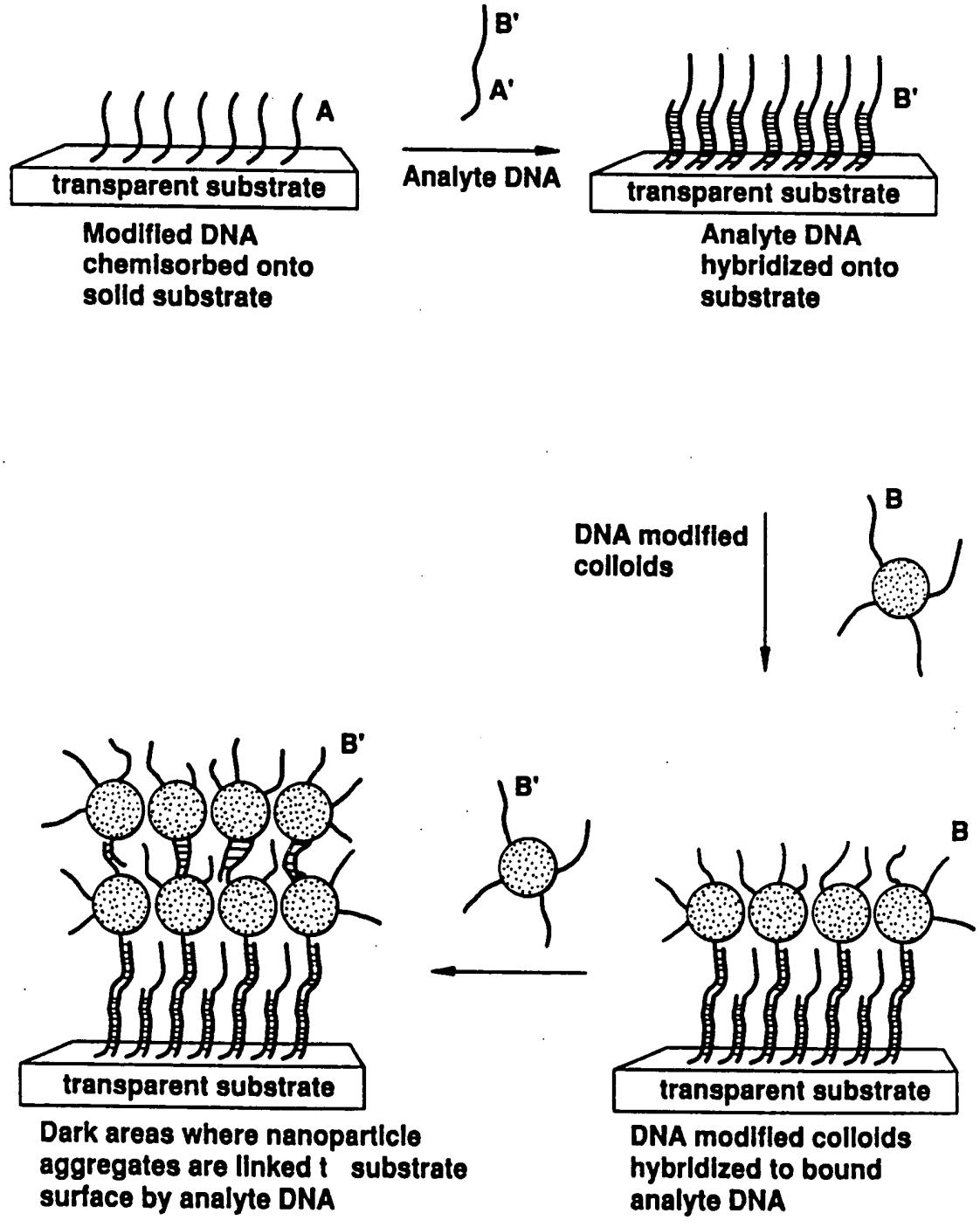


FIG. 13B

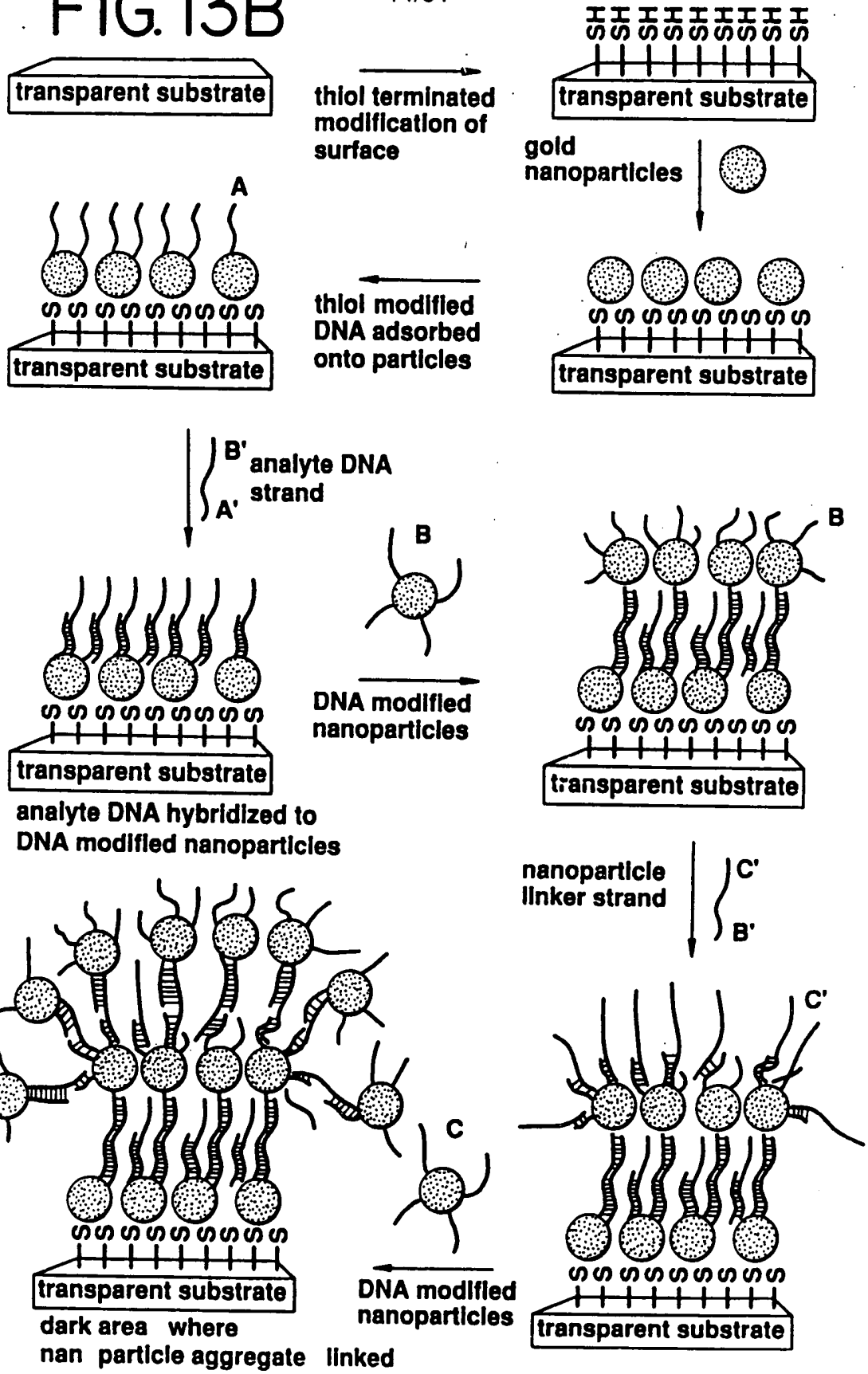

transparent substrate
thiol terminated modification of surface
transparent substrate
gold nanoparticles
A
thiol modified DNA adsorbed onto particles
transparent substrate
transparent substrate
B' analyte DNA strand
A'
B
DNA modified nanoparticles
B
transparent substrate
transparent substrate
analyte DNA hybridized to DNA modified nanoparticles
nanoparticle linker strand
C'
B'
C'
C
transparent substrate
DNA modified nanoparticles
transparent substrate
dark area where nan particle aggregate linked to substrate by analyte DNA

FIG. 14A

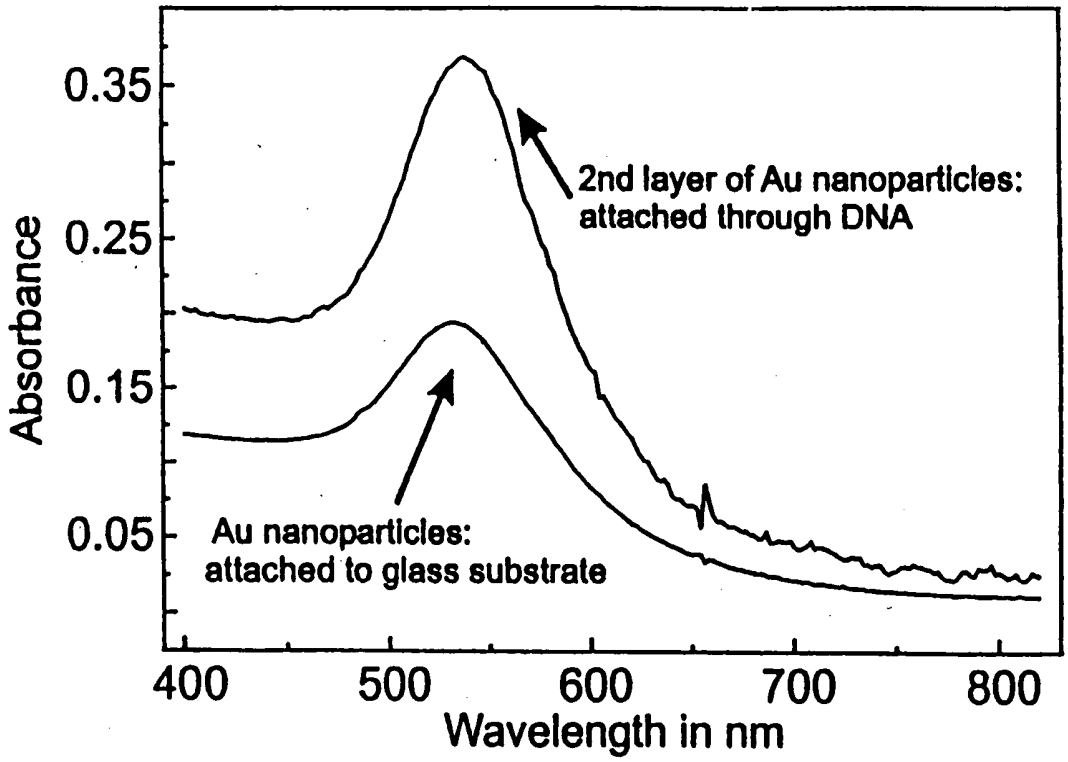


FIG. 14B

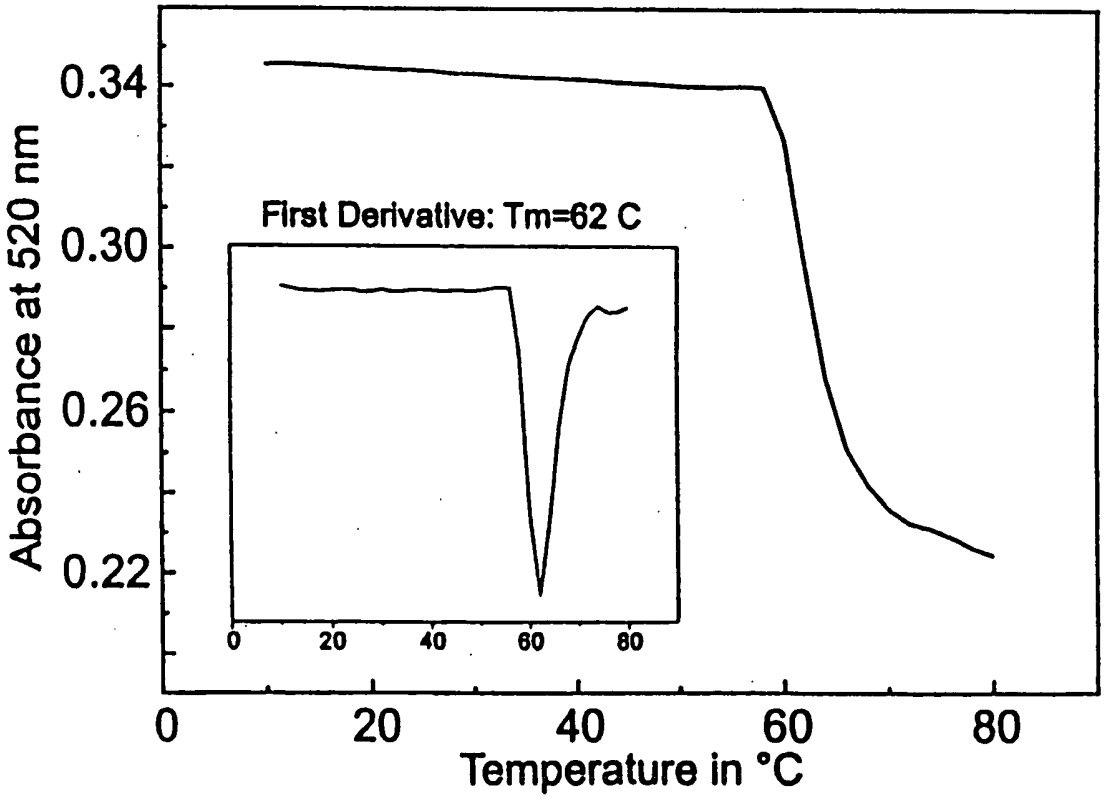


FIG. 15A

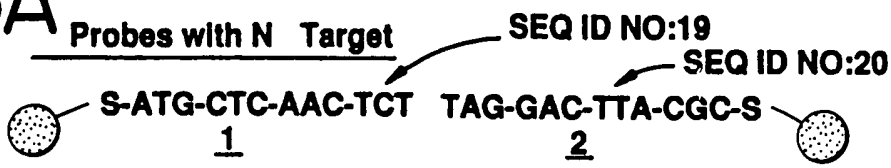


FIG. 15B

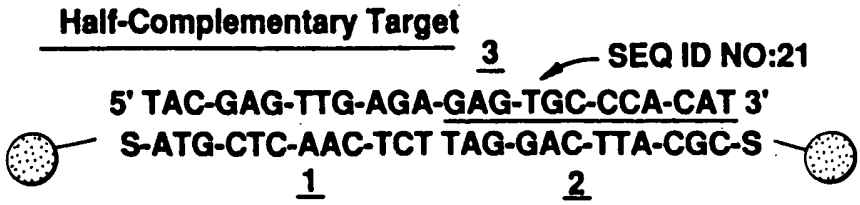


FIG. 15C

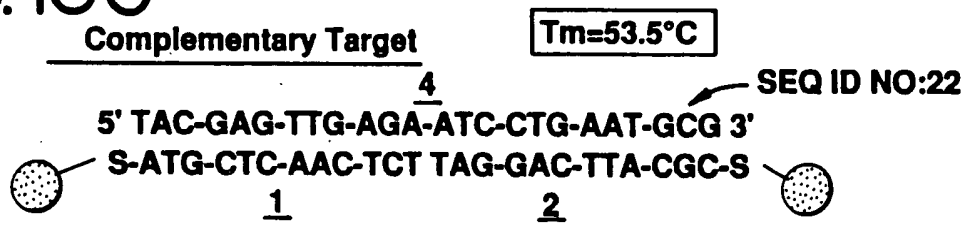


FIG. 15D

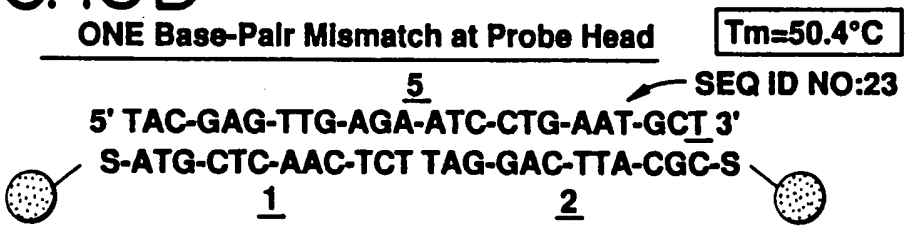


FIG. 15E

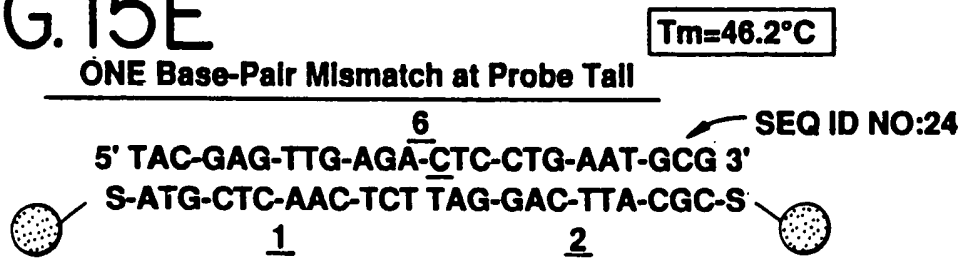


FIG. 15F

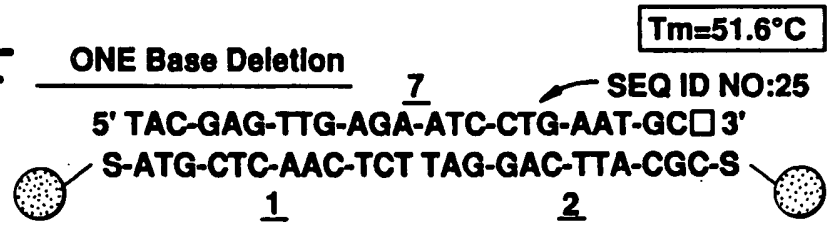


FIG. 15G

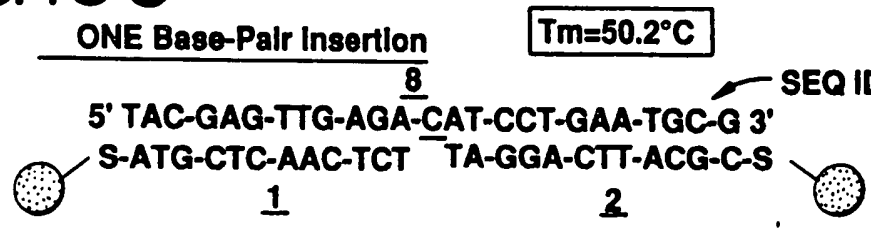


FIG. 16A

24 Base Template

5' TAC-GAG-TTG-AGA-ATC-CTG-AAT-GCG 3'
S-ATG-CTC-AAC-TCT TAG-GAC-TTA-CGC-S
1 2

FIG. 16B

48 Base Template with Complementary 24 Base Filler

5' TAC-GAG-TTG-AGA-CCG-TTA-AGA-CGA-GGC-AAT-CAT-GCA-ATC-CTG-AAT-GCG 3'
S-ATG-CTC-AAC-TCT GGC-AAT-TCT-GCT-CCG-TTA-GTA-CGT TAG-GAC-TTA-CGC-S
1 2

FIG. 16C

72 Base Template with Complementary 48 Base Filler

5' TAC-GAG-TTG-AGA-CCG-TTA-AGA-CGA-GGC-AAT-CAT-GCA-TAT-ATT-GGA-CGC-TTT-ACG-GAC-AAC-ATC-CTG-AAT-GCG 3'
S-ATG-CTC-AAC-TCT GGC-AAT-TCT-GCT-CCG-TTA-GTA-CGT-ATA-TAA-CCT-GCG-AAA-TGC-CTG-TTG TAG-GAC-TTA-CGC-S
1 2

FIG. 17A

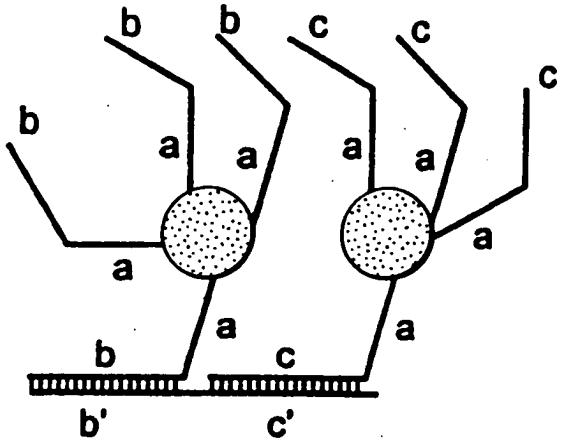


FIG. 17B

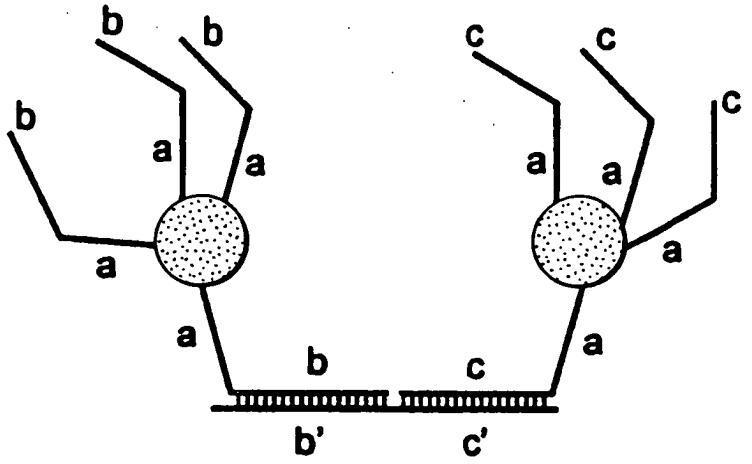


FIG. 17C

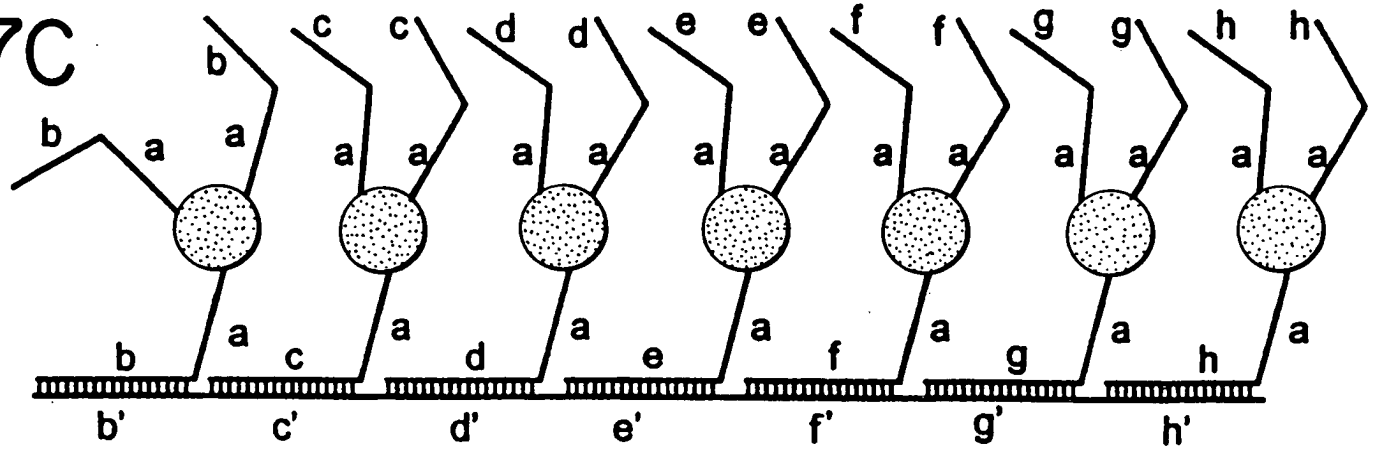


FIG. 17D

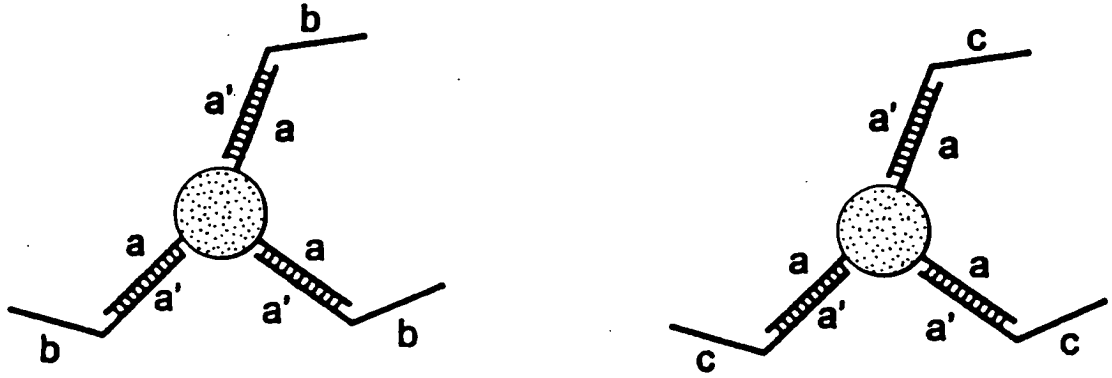


FIG. 17E

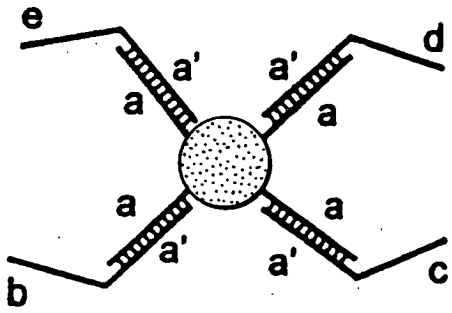


FIG. 18

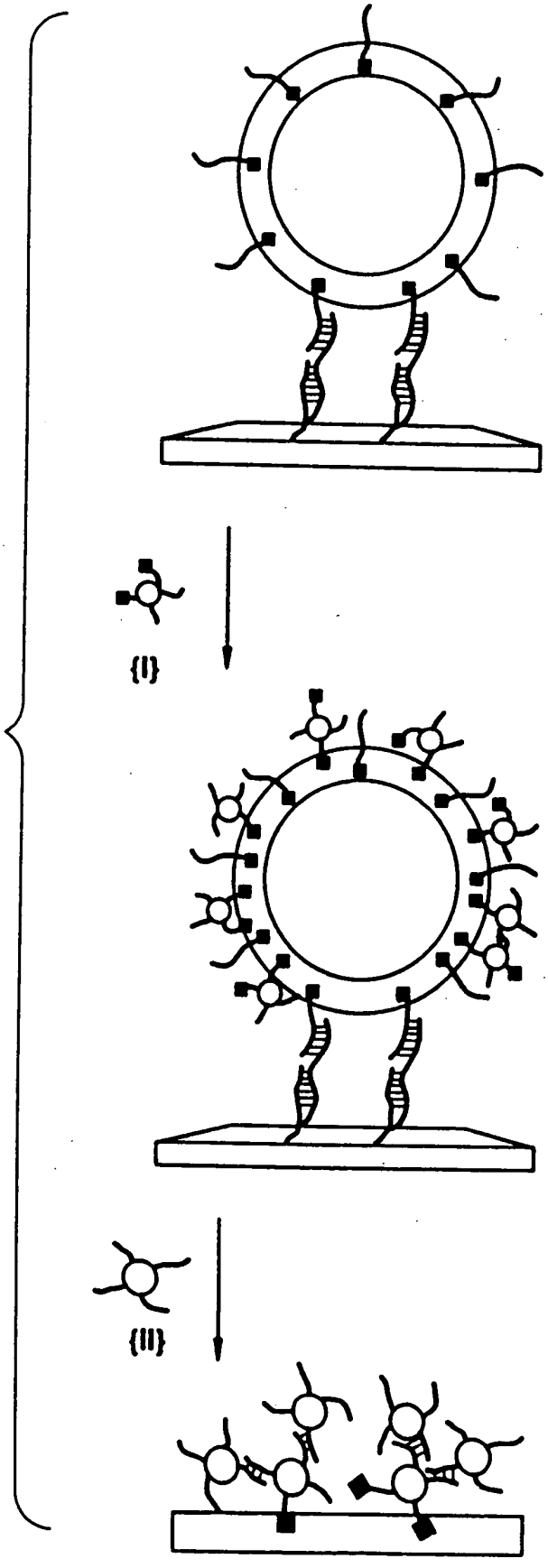


FIG. 19A

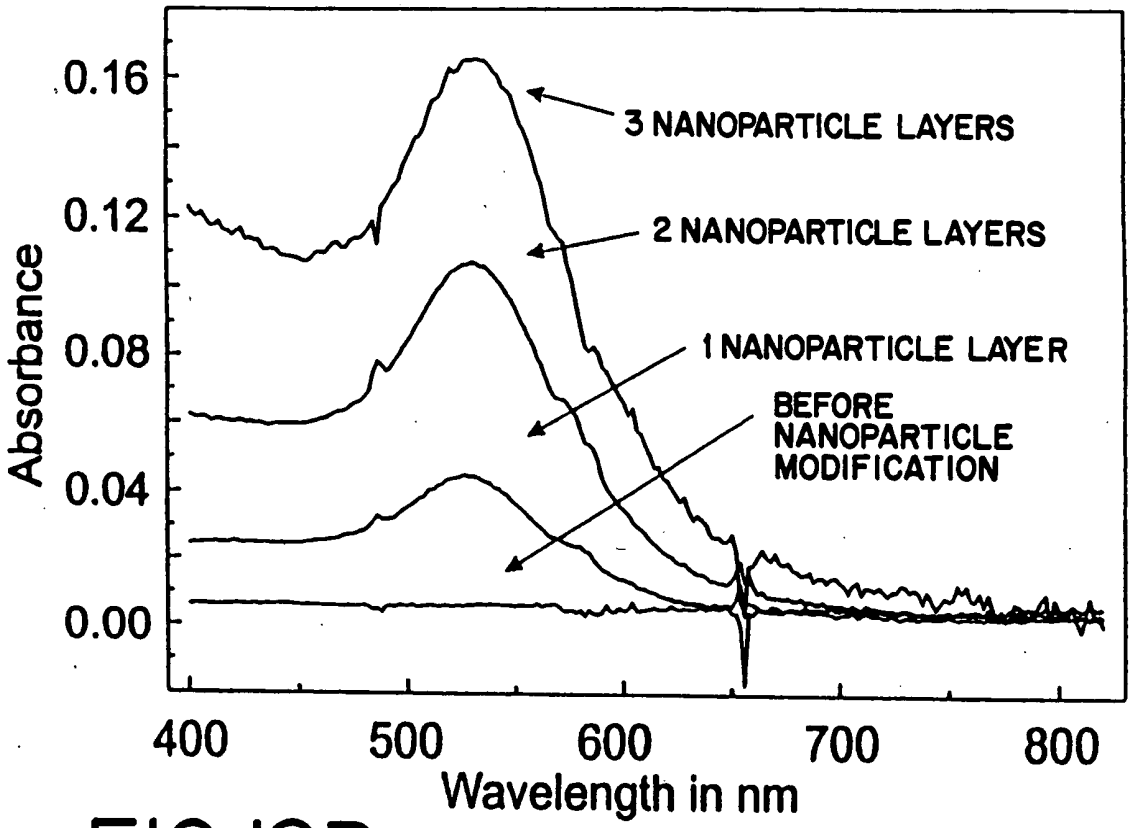


FIG. 19B

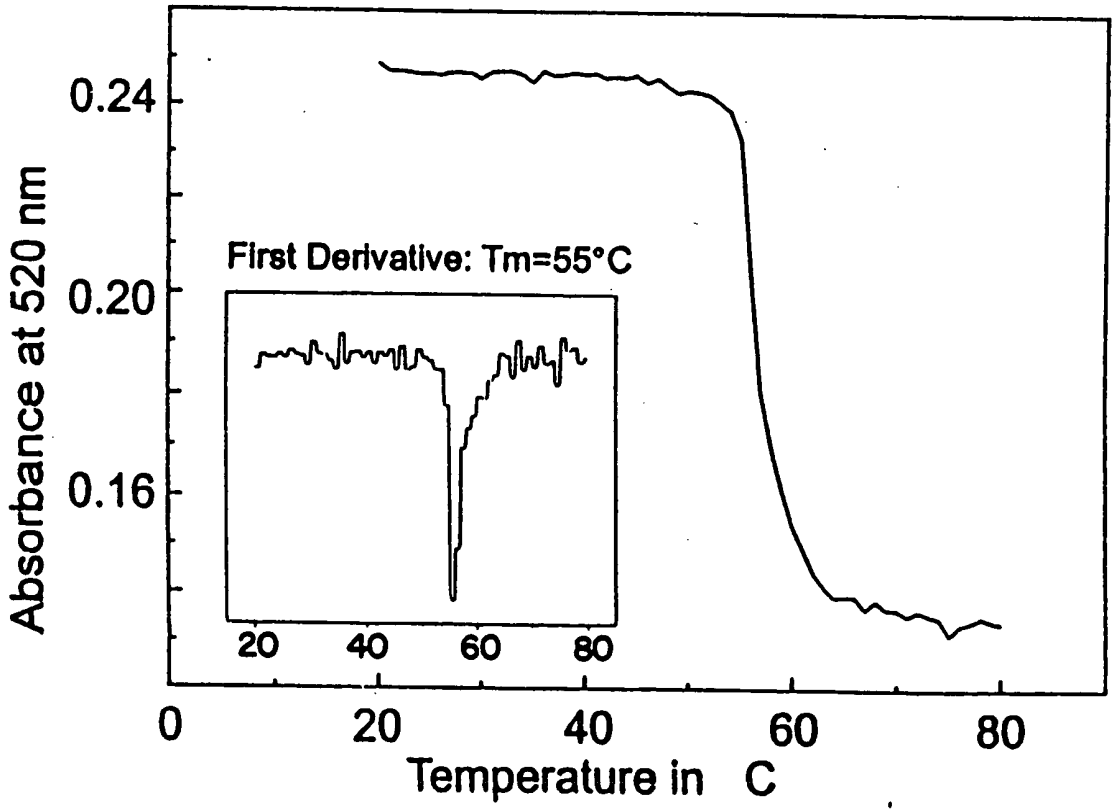


FIG. 20A

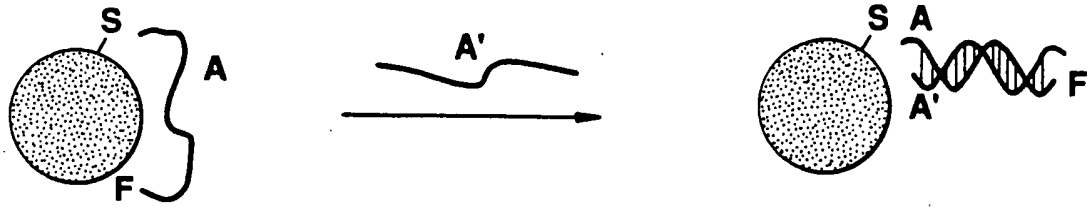


FIG. 20B

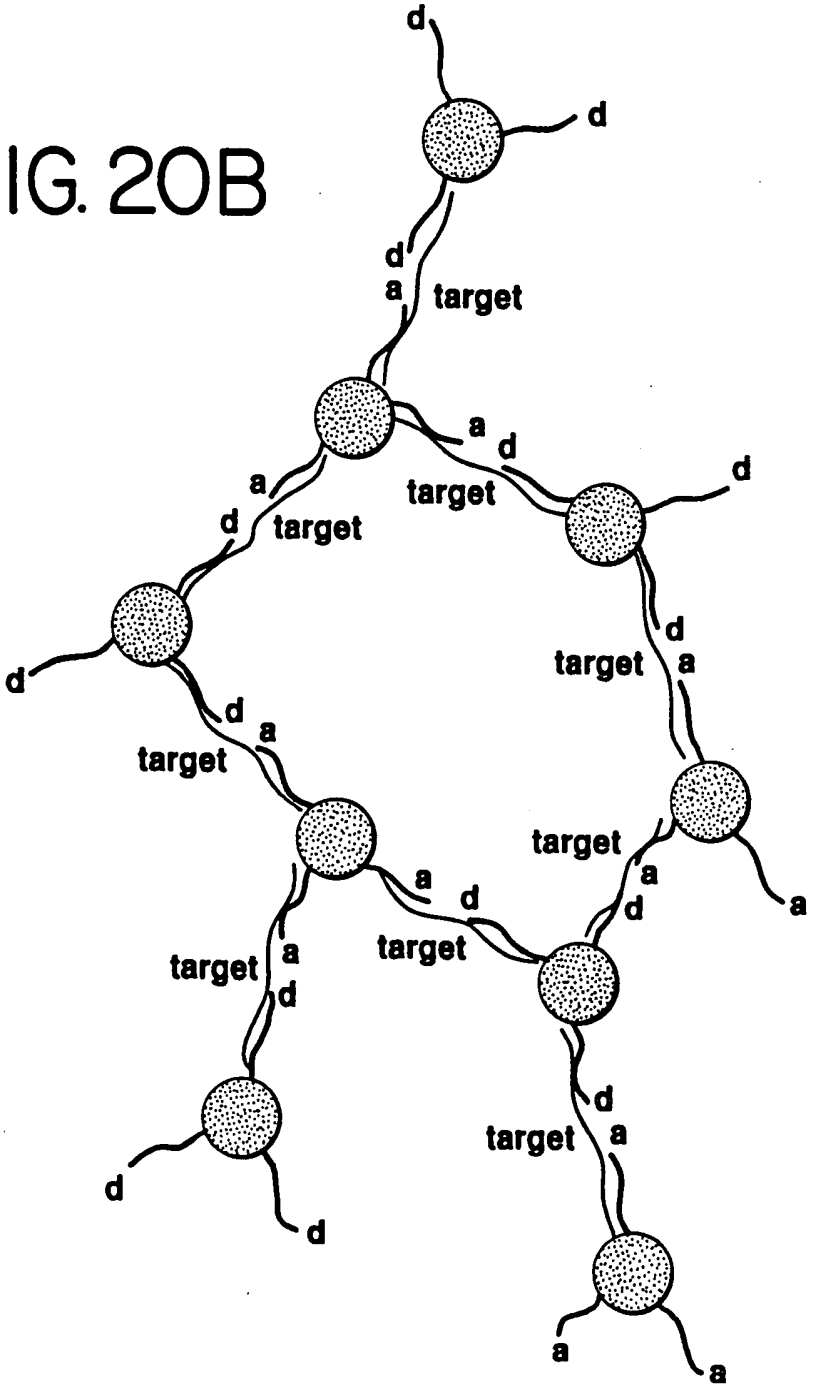


FIG. 21

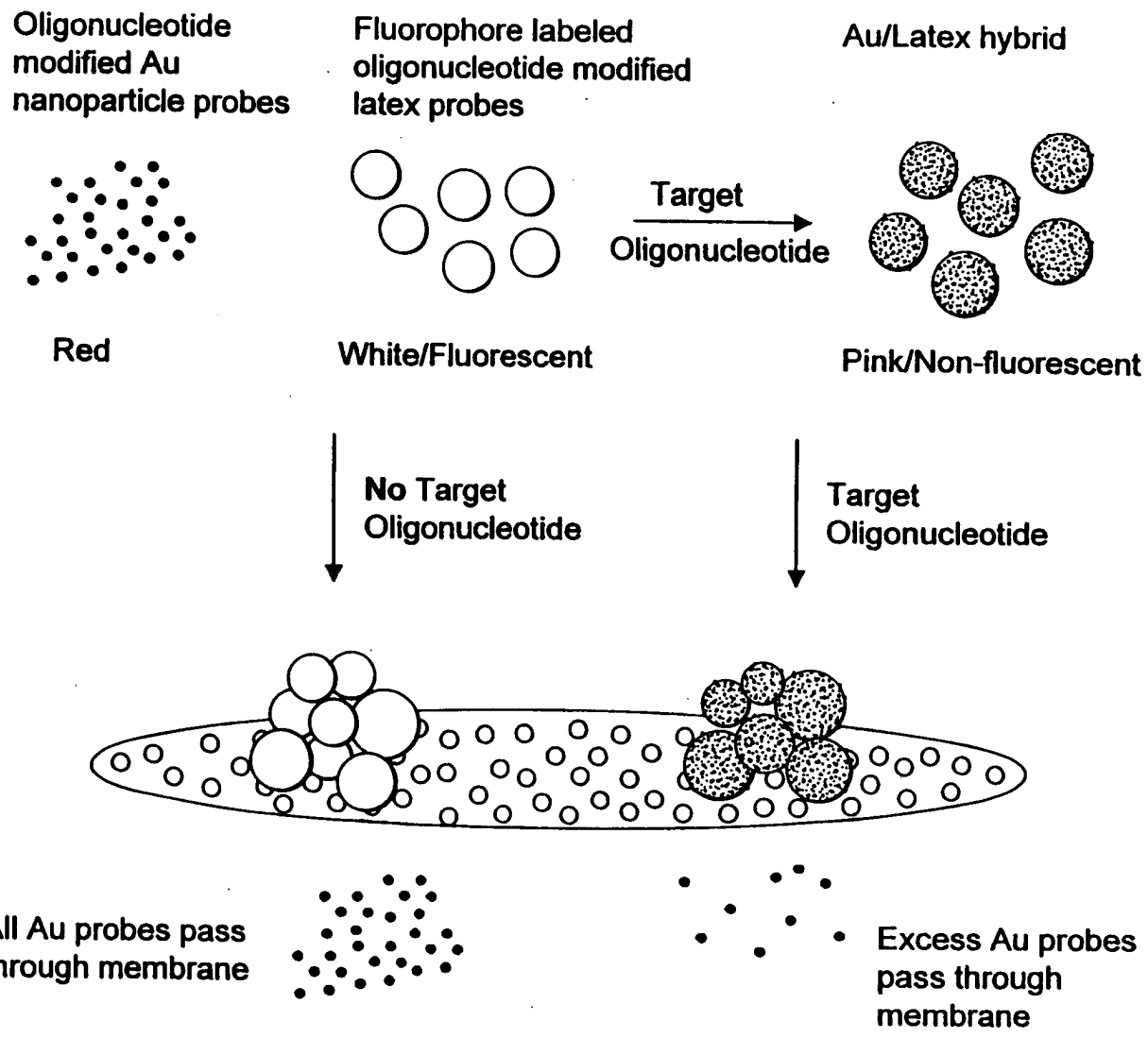
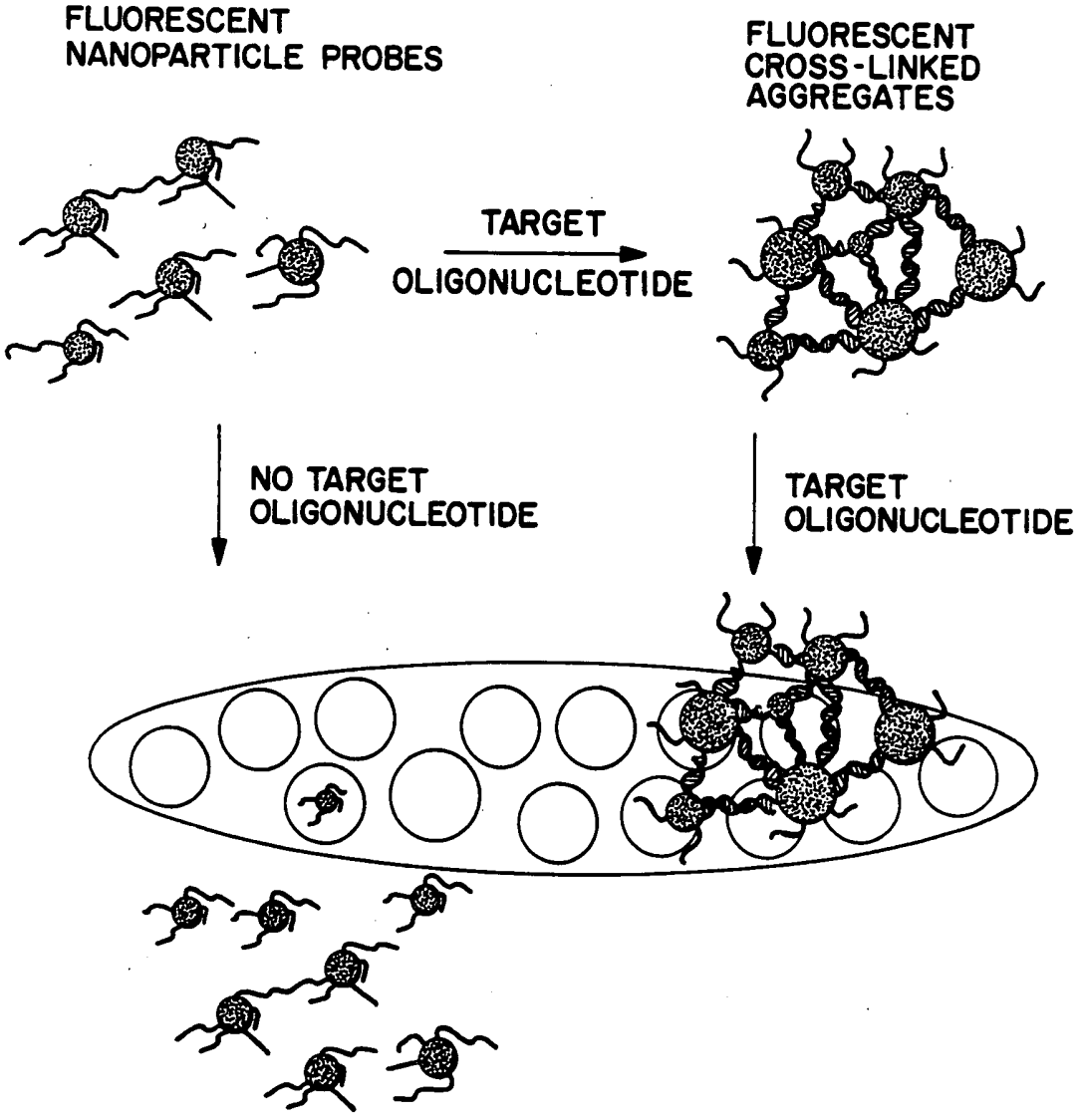

Oligonucleotide modified Au nanoparticle probes
Fluorophore labeled oligonucleotide modified latex probes
Au/Latex hybrid
Target Oligonucleotide
Red
White/Fluorescent
Pink/Non-fluorescent
No Target Oligonucleotide
Target Oligonucleotide
All Au probes pass through membrane
Excess Au probes pass through membrane

FIG. 22



THE FLUORESCENT NANOPARTICLE PROBES PASS THROUGH THE MEMBRANE

THE FLUORESCENT CROSS-LINKED AGGREGATES ARE RETAINED BY THE MEMBRANE

FIG. 23

Anthrax PCR Product

5'G GCG GAT GAG TCA GTA GTT AAG GAG GCT CAT AGA GAA GTA ATT AAT
3'C CGC CTA CTC AGT CAT CAA TTC CTC CGA GTA TCT CTT CAT TAA TTA

TCG TCA ACA GAG GGA TTA TTG TTA AAT ATT GAT AAG GAT ATA AGA AAA
AGC AGT TGT CTC CCT AAT AAC AAT TTA TAA CTA TTC CTA TAT TCT TTT

ATA TTA TCC AGG GTT ATA TTG TAG AAA TTG AAG ATA CTG AAG GGC TT 3'
TAT AAT AGG TCC CAA TAT AAC ATC TTT AAC TTC TAT GAC TTC CCG AA 5'

141 mer Anthrax PCR product [SEQ ID NO:36]

[SEQ ID NO:37]

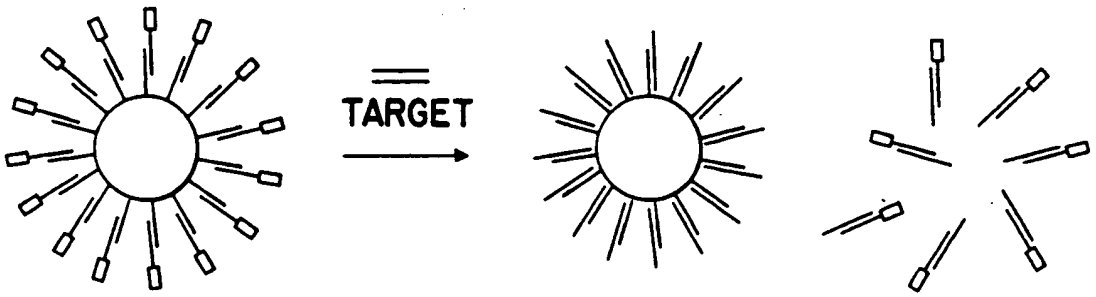
[SEQ ID NO:38]

Oligonucleotide-Nanoparticle Probes

Blocker Oligonucleotides

3' C CGC CTA CTC AGT CAT CAA TTC CTC CGA GT	[SEQ ID NO:39]
3' A TCT CTT CAT TAA TTA AGC AGT TGT	[SEQ ID NO:40]
3' TAT TCT TTT TAT AAT AGG TCC CAA TAT	[SEQ ID NO:41]
3' AAC ATC TTT AAC TTC TAT GAC TTC CCG AA	[SEQ ID NO:42]

FIG. 24


TARGET
SATELLITE PROBE
DETECTION SIGNAL

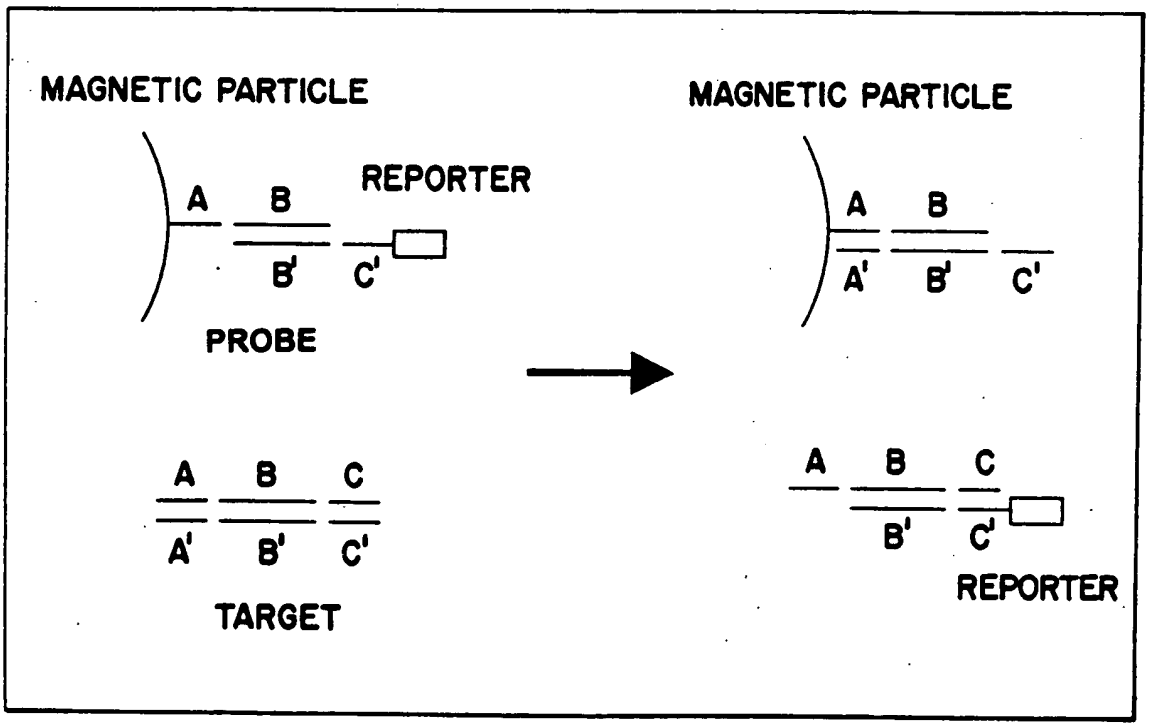

MAGNETIC PARTICLE
A
B
REPORTER
B'
C'
PROBE
A
B
C
A'
B'
C'
TARGET
MAGNETIC PARTICLE
A
B
A'
B'
C'
A
B
C
B'
C'
REPORTER

FIG. 25A

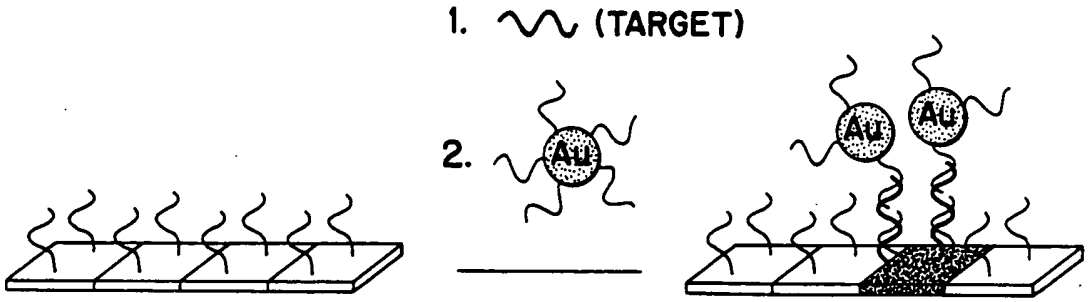


FIG. 25B

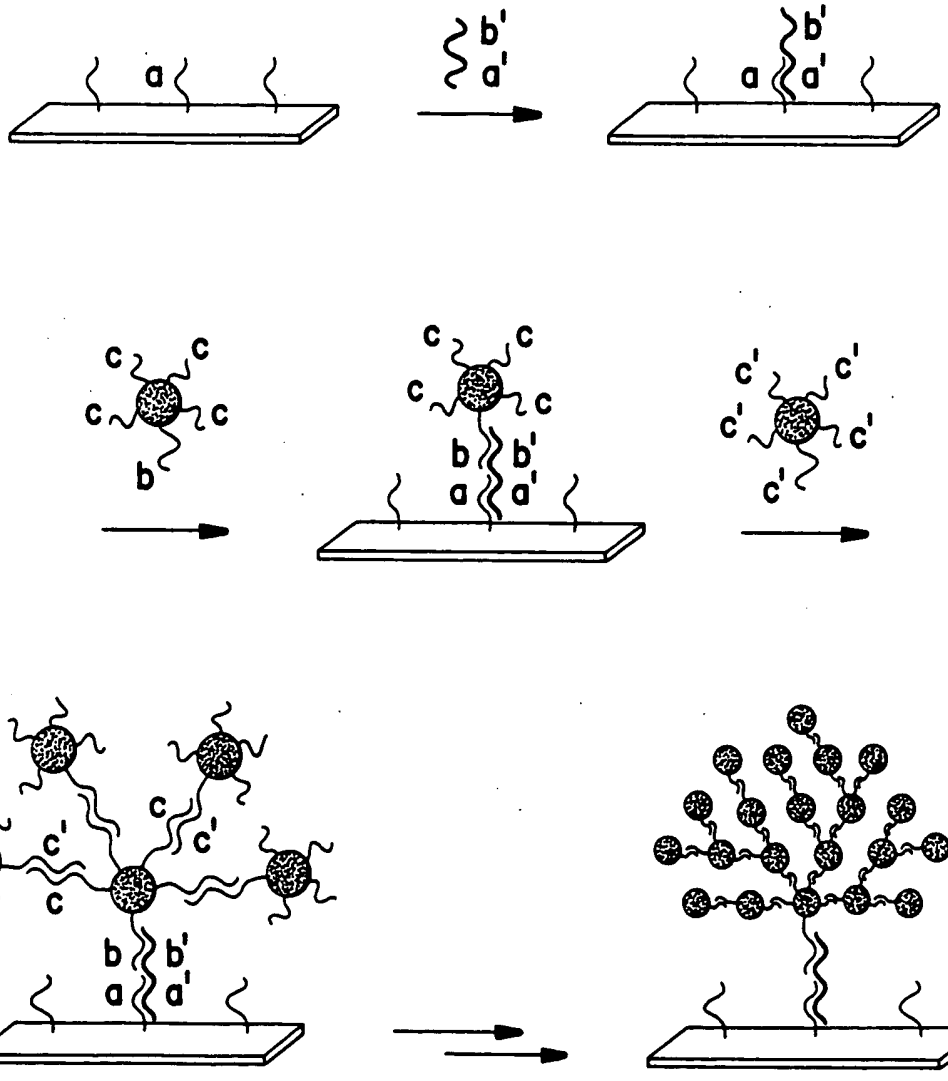


FIG. 26A

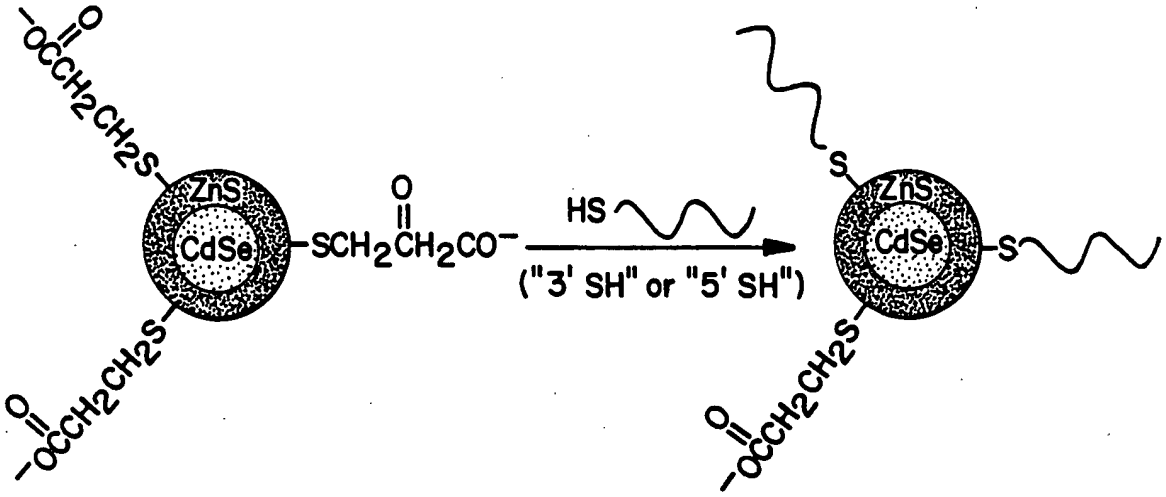


FIG. 26B

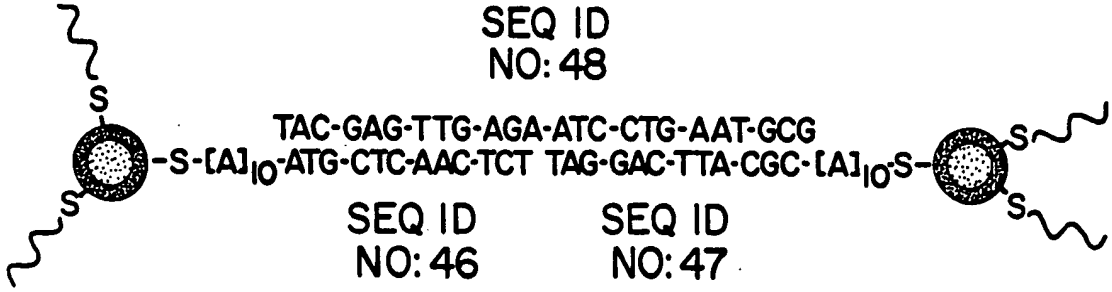


FIG. 27A

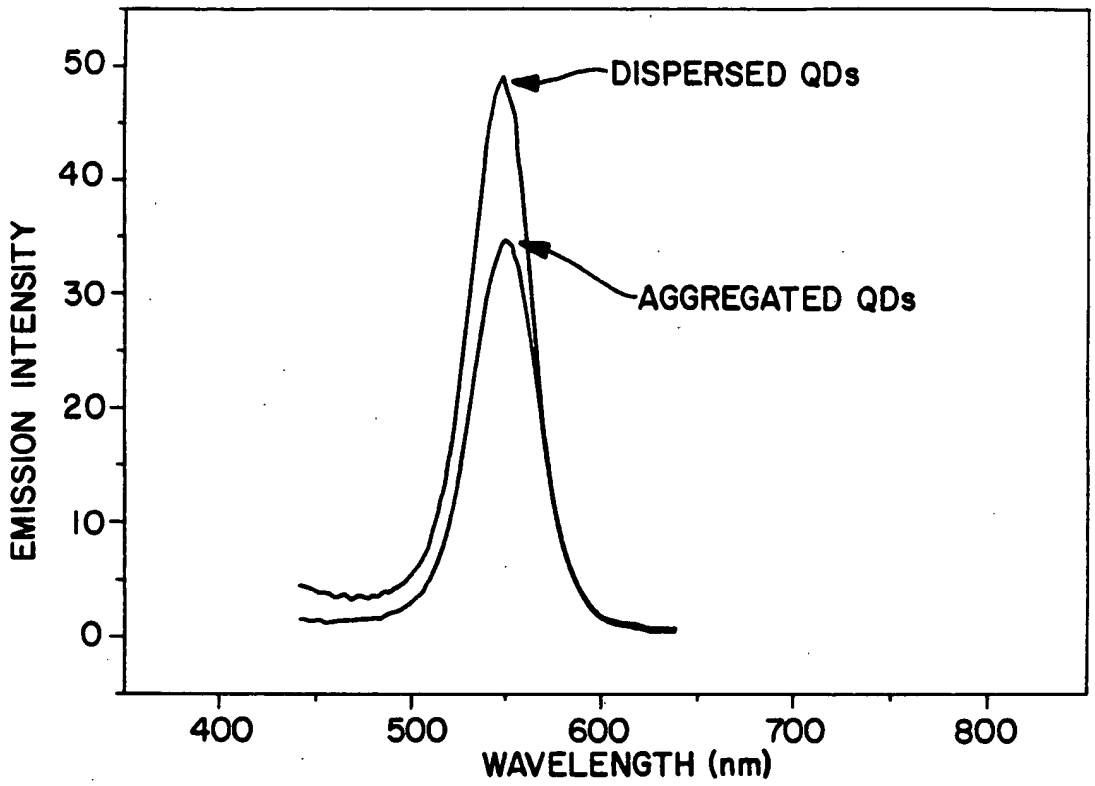


FIG. 27B

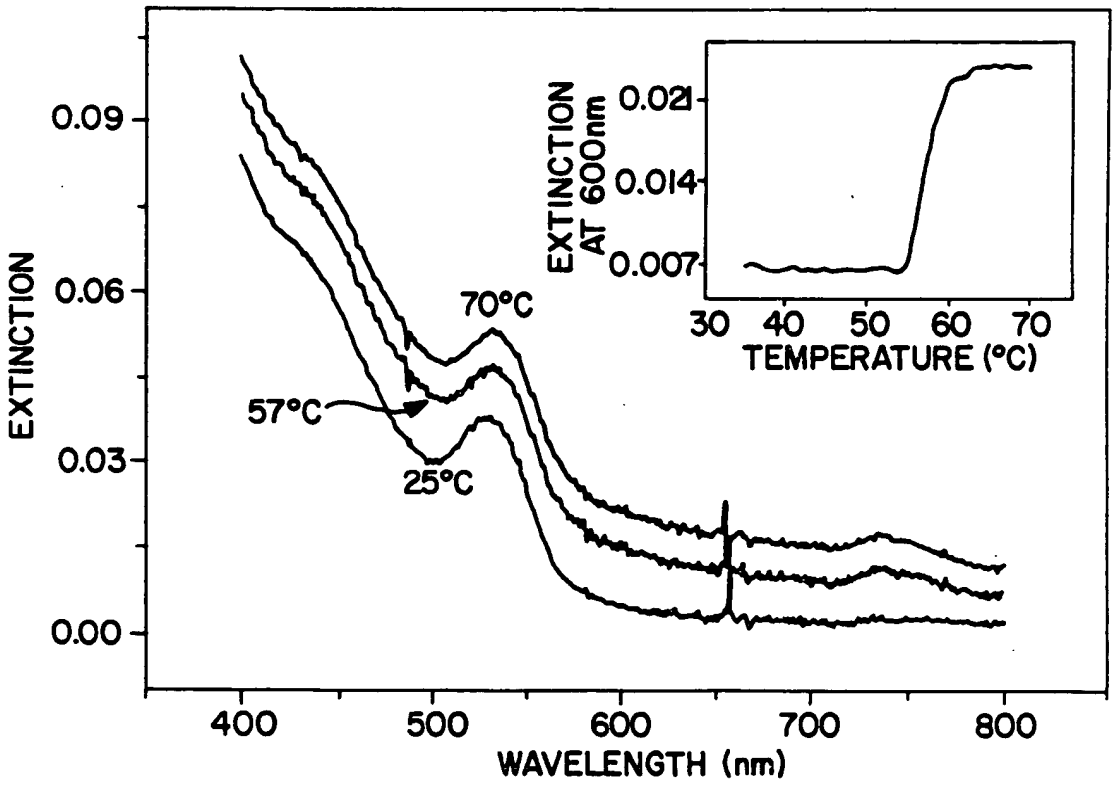


FIG. 27C

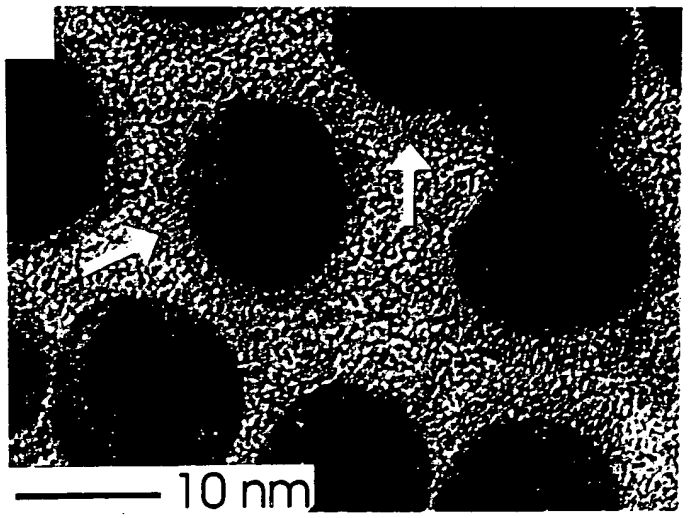


FIG. 27D

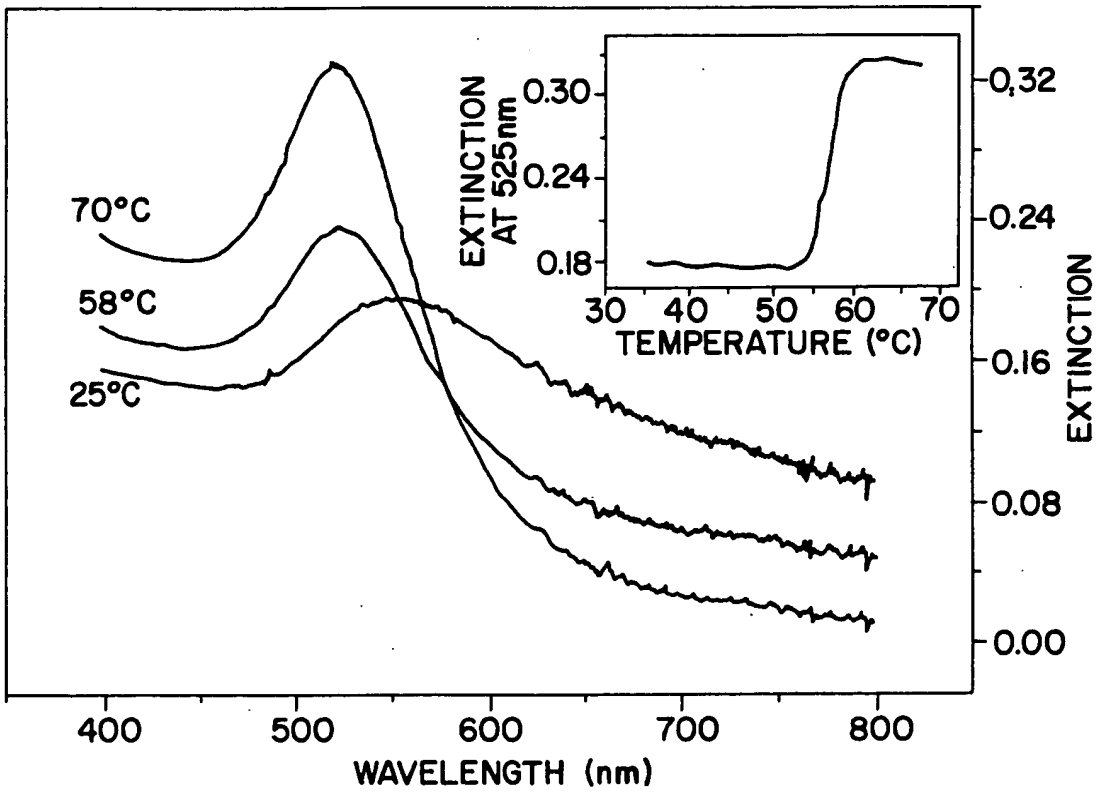


FIG. 28A

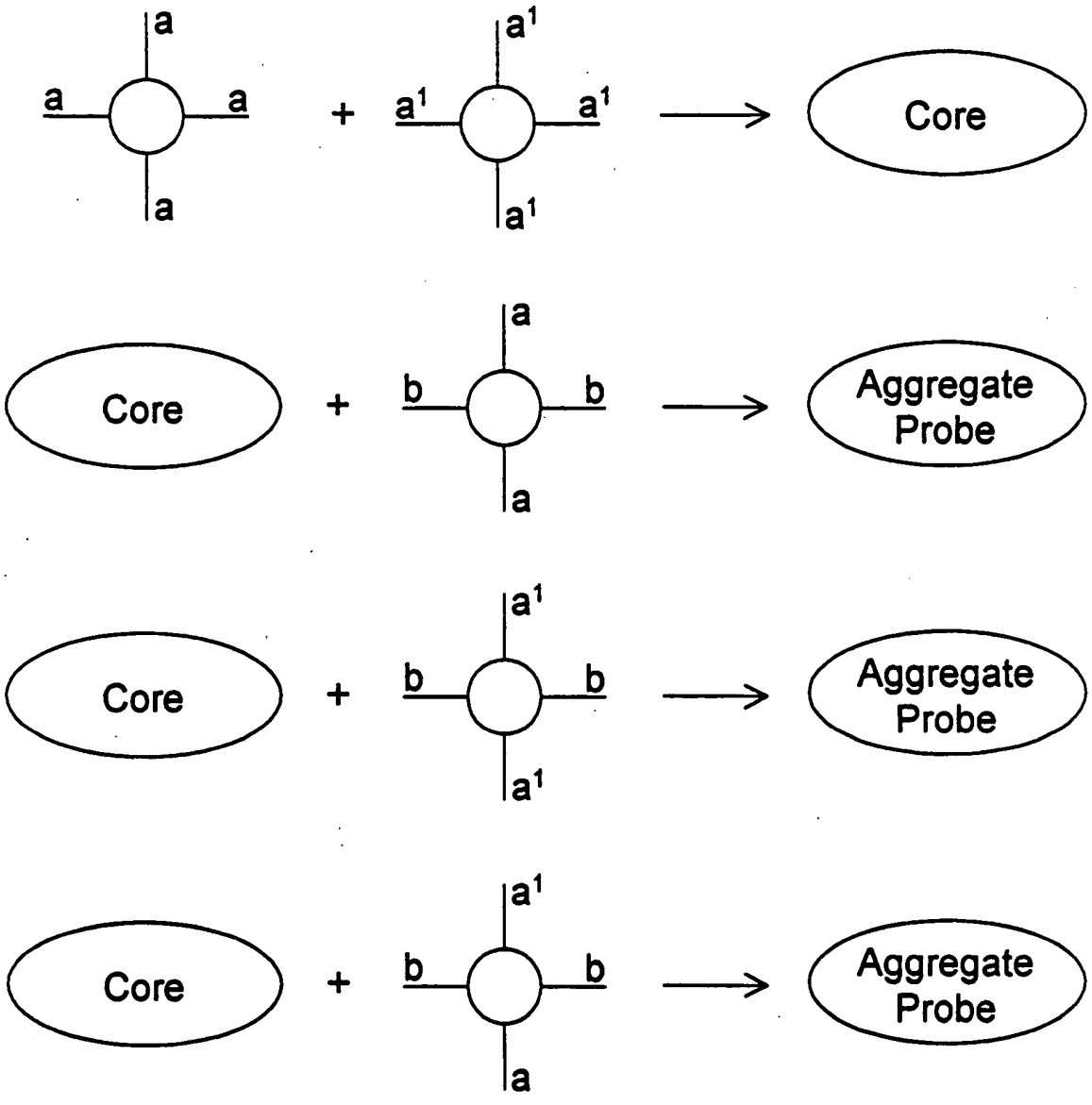

a
a
a
a
+
a1
a1
a1
a1
Core
Core
+
a
b
b
a
Aggregate Probe
Core
+
a1
b
b
a1
Aggregate Probe
Core
+
a1
b
b
a
Aggregate Probe

FIG. 28B

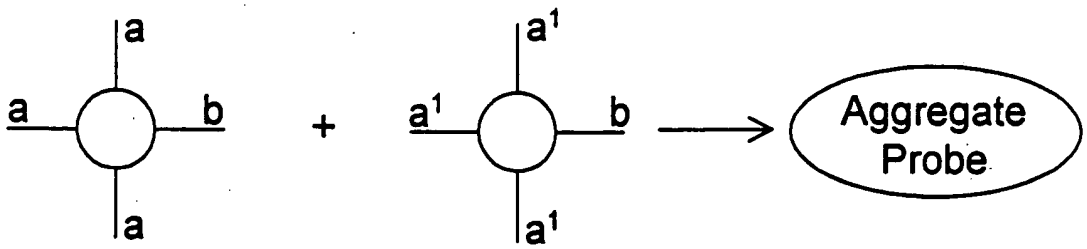


FIG. 28C

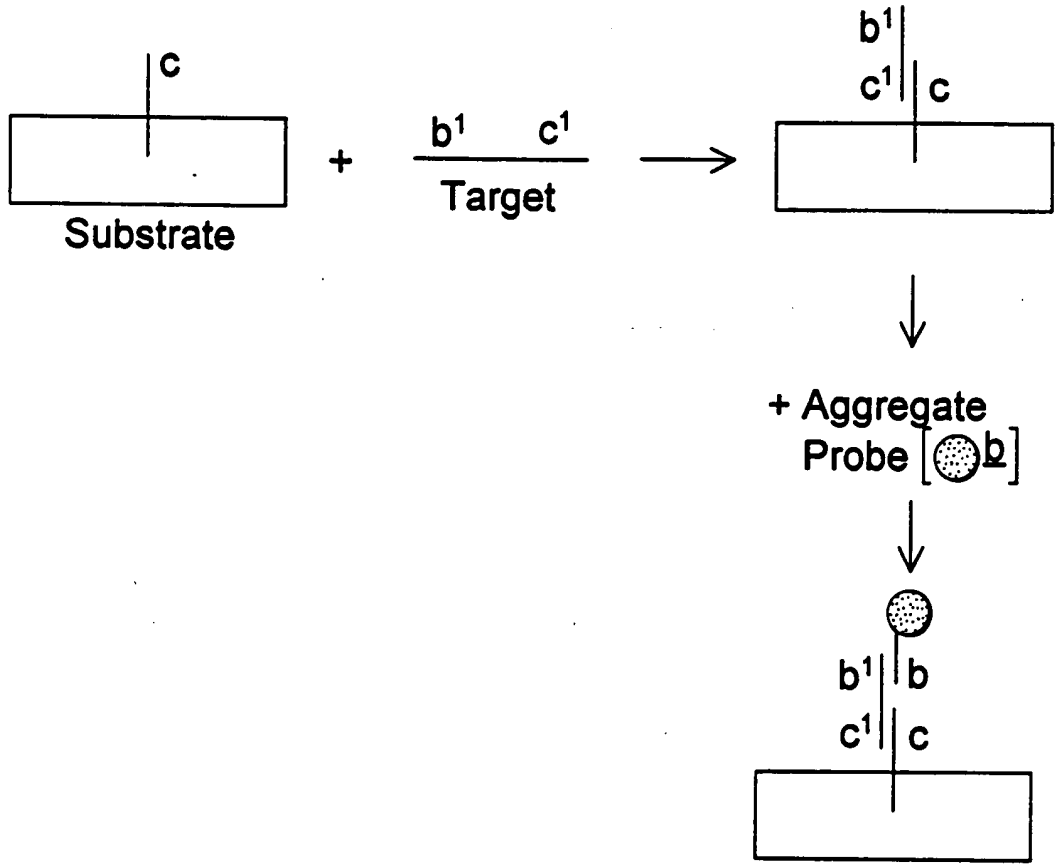


FIG. 28D

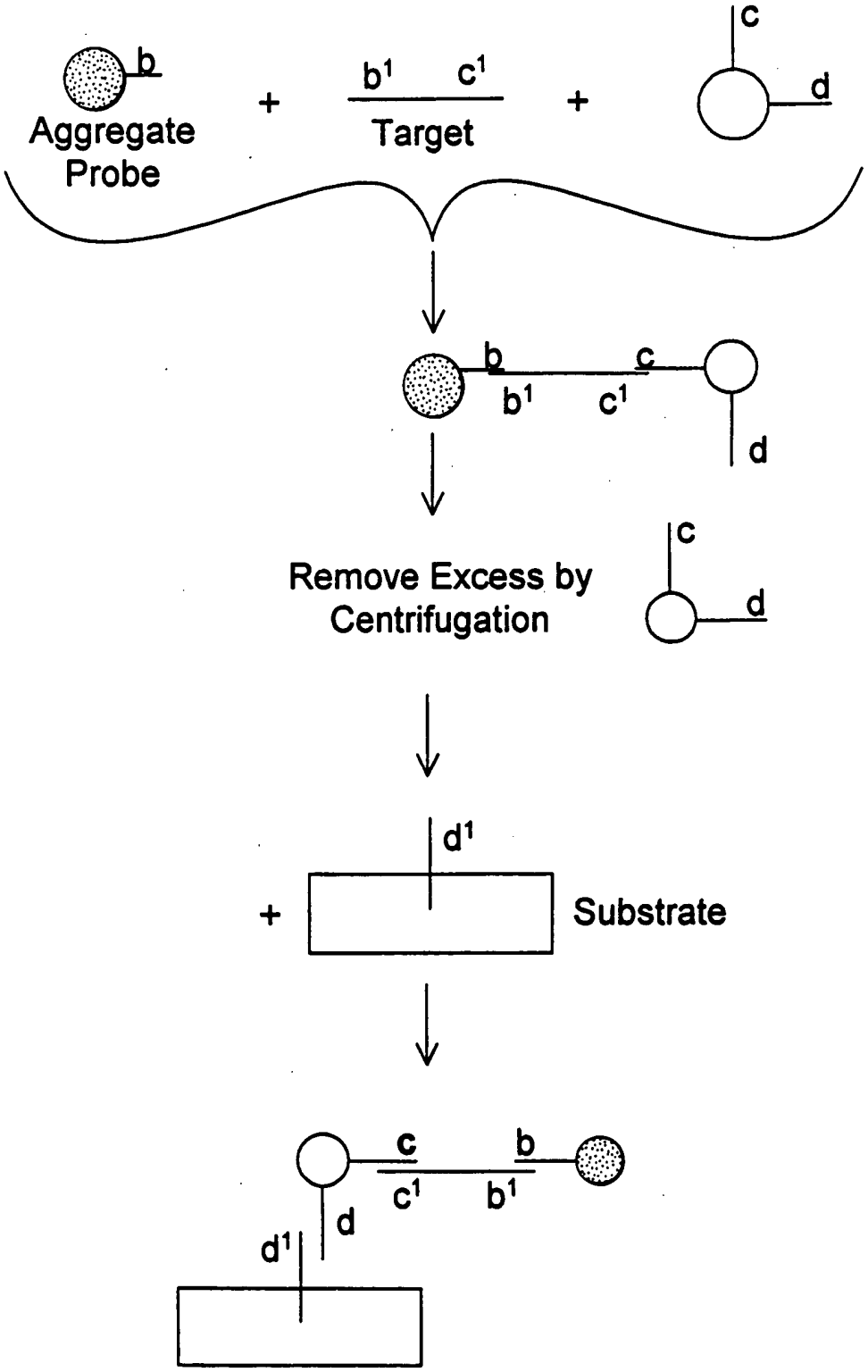

b
Aggregate Probe
+
b1 c1
Target
+
c
d
b
c
b1
c1
d
Remove Excess by Centrifugation
c
d
d1
+
Substrate
c
b
c1
b1
d
d1

FIG. 28E

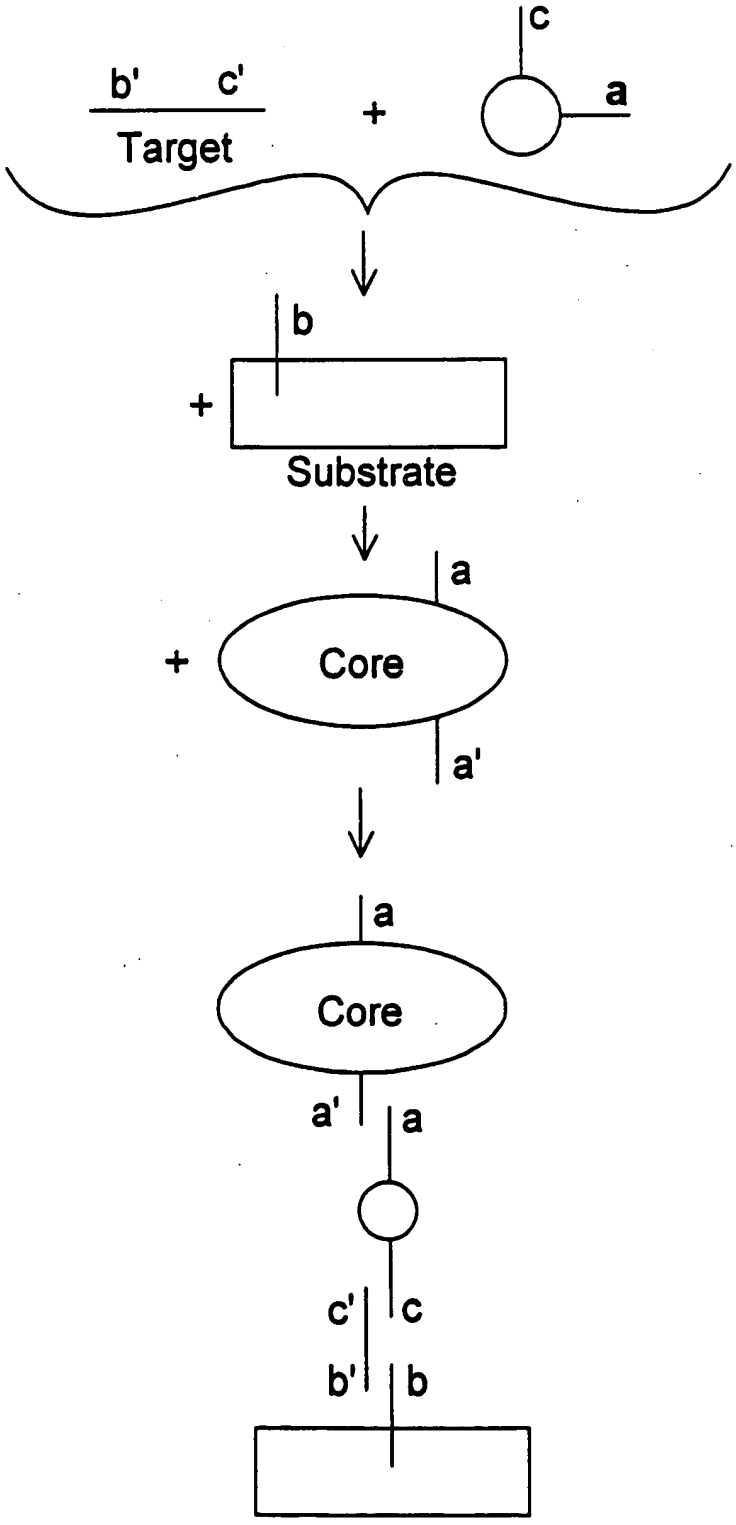


FIG. 29

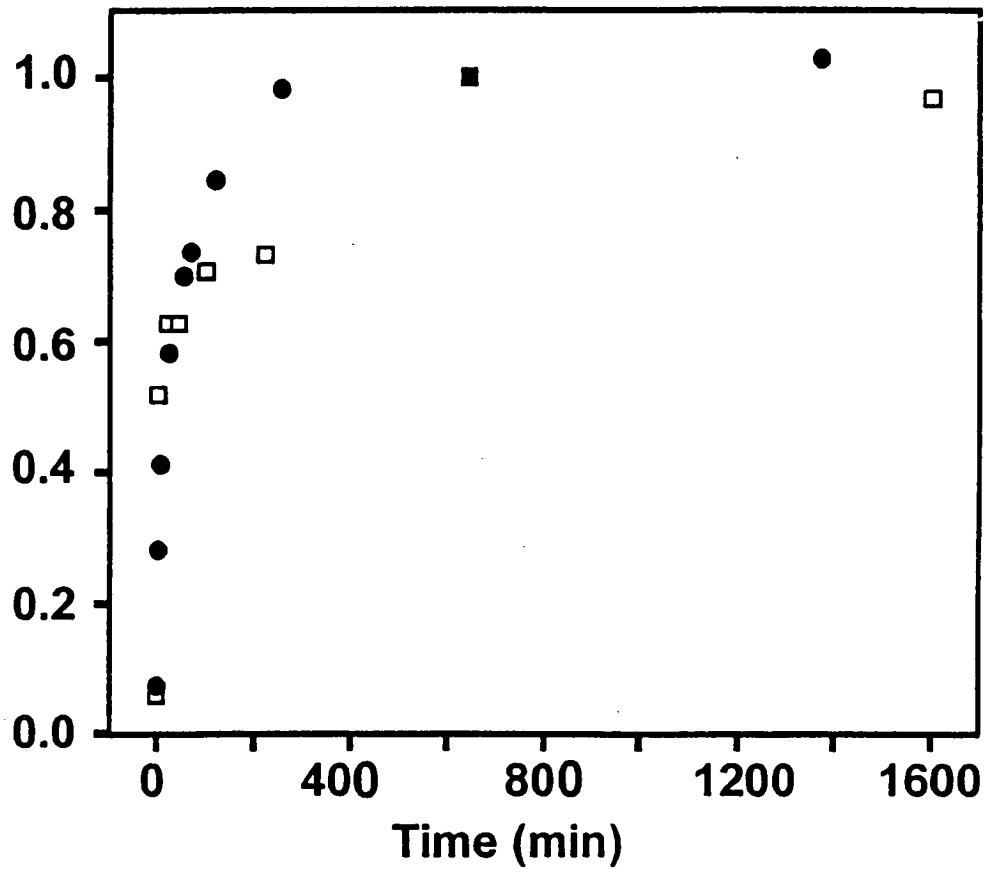

Fractional Displacement by ME
1.0
0.8
0.6
0.4
0.2
0.0
0
400
800
1200
1600
Time (min)

FIG. 30

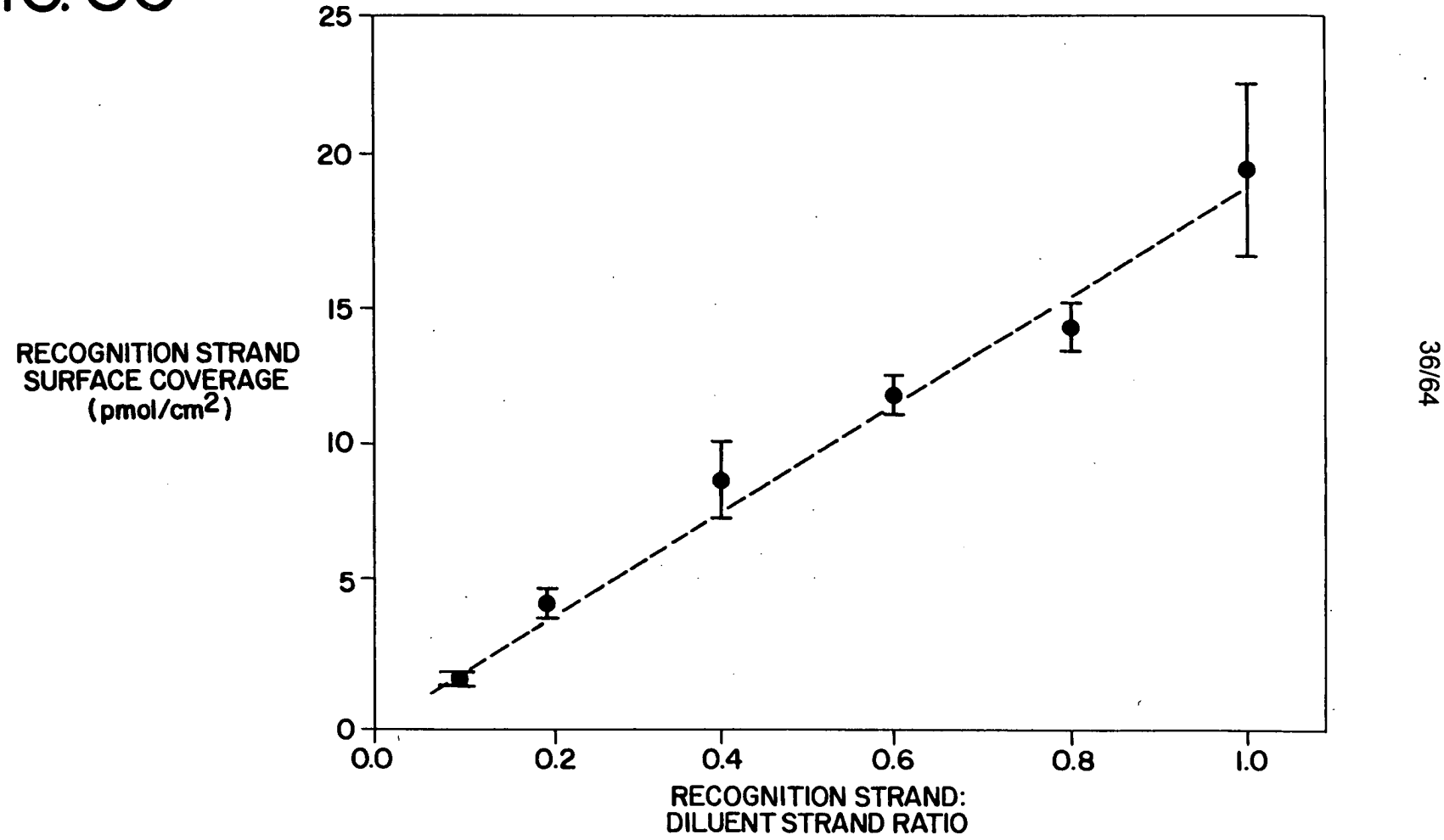

RECOGNITION STRAND SURFACE COVERAGE (pmol/cm2)
25
20
15
10
5
0
0.0
0.2
0.4
0.6
0.8
1.0
RECOGNITION STRAND: DILUENT STRAND RATIO

FIG. 31

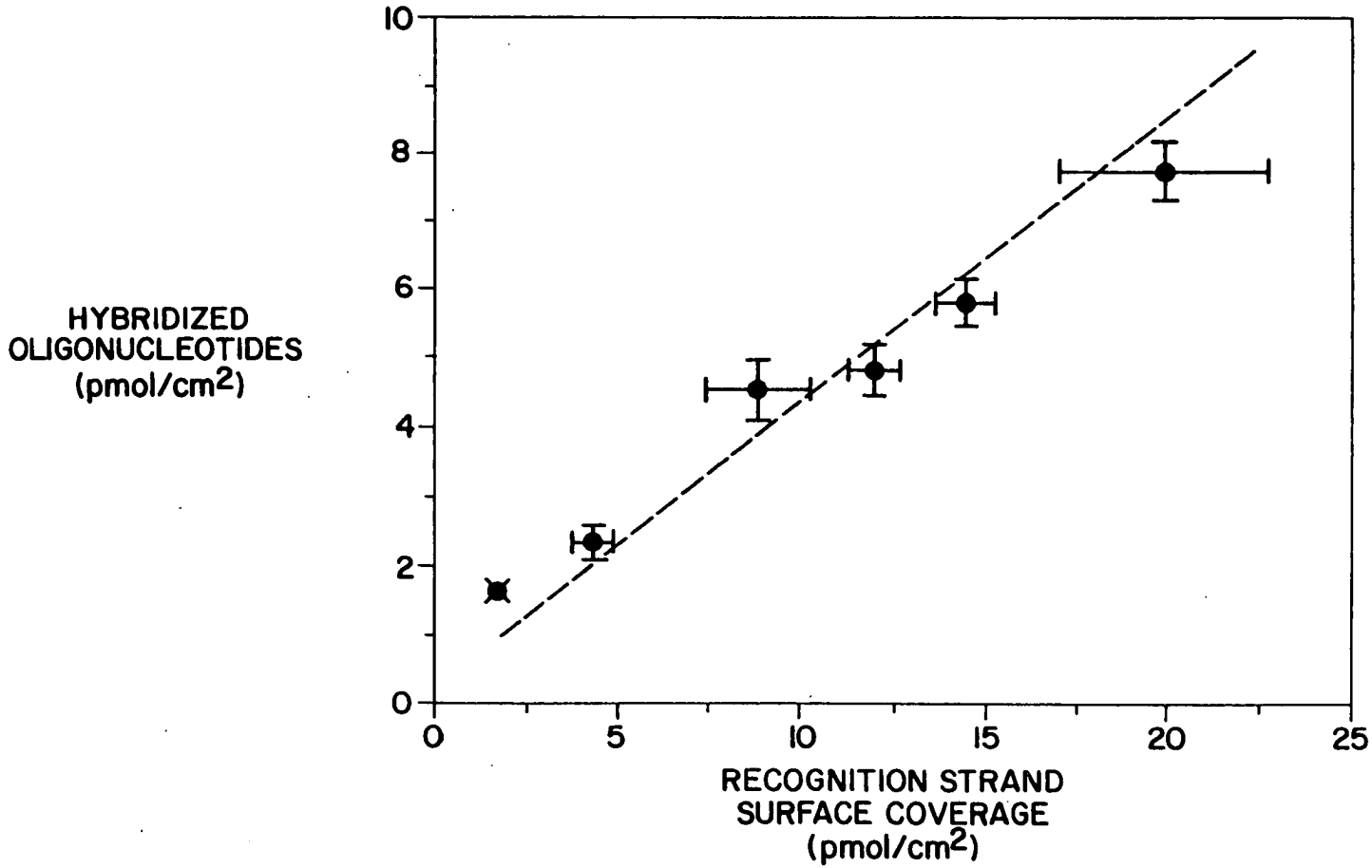
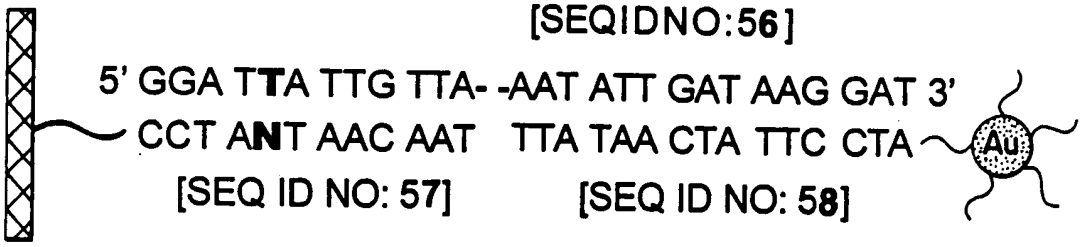

HYBRIDIZED
OLIGONUCLEOTIDES
(pmol/cm2)
10
8
6
4
2
0
0
5
10
15
20
25
RECOGNITION STRAND
SURFACE COVERAGE
(pmol/cm2)

FIG. 32



N = A (complementary),
G,C,T (mismatched)

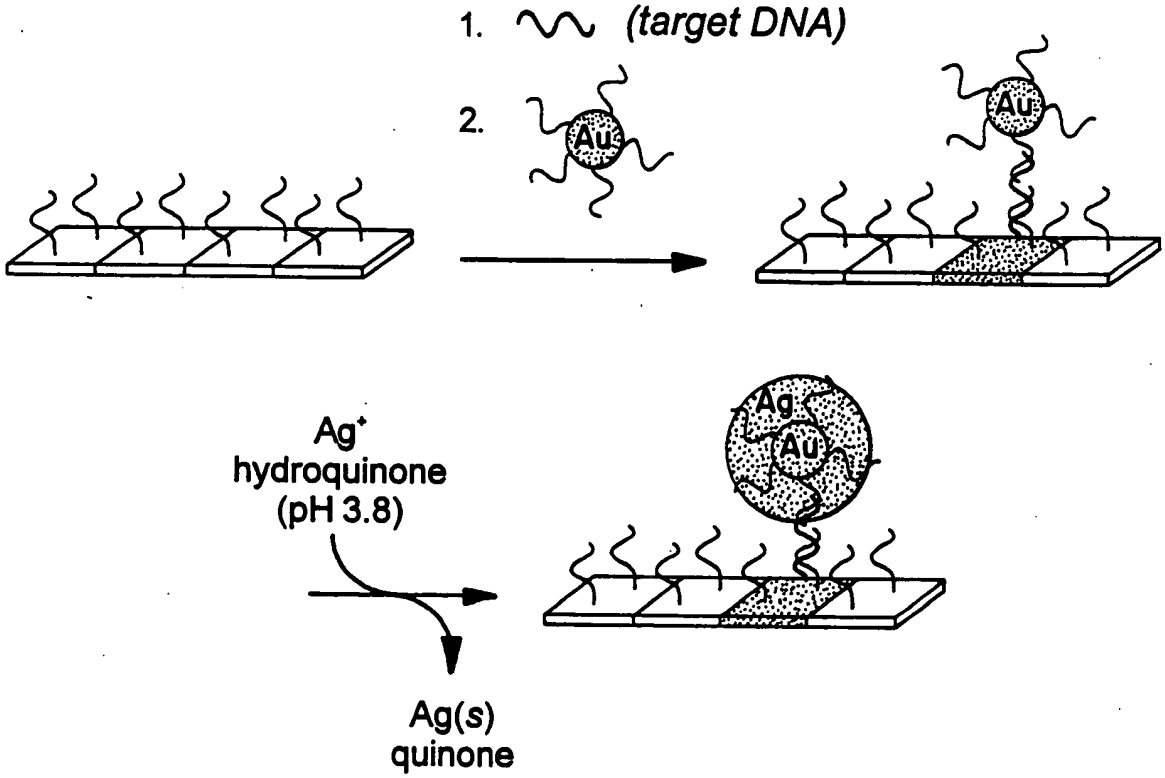


FIG. 33

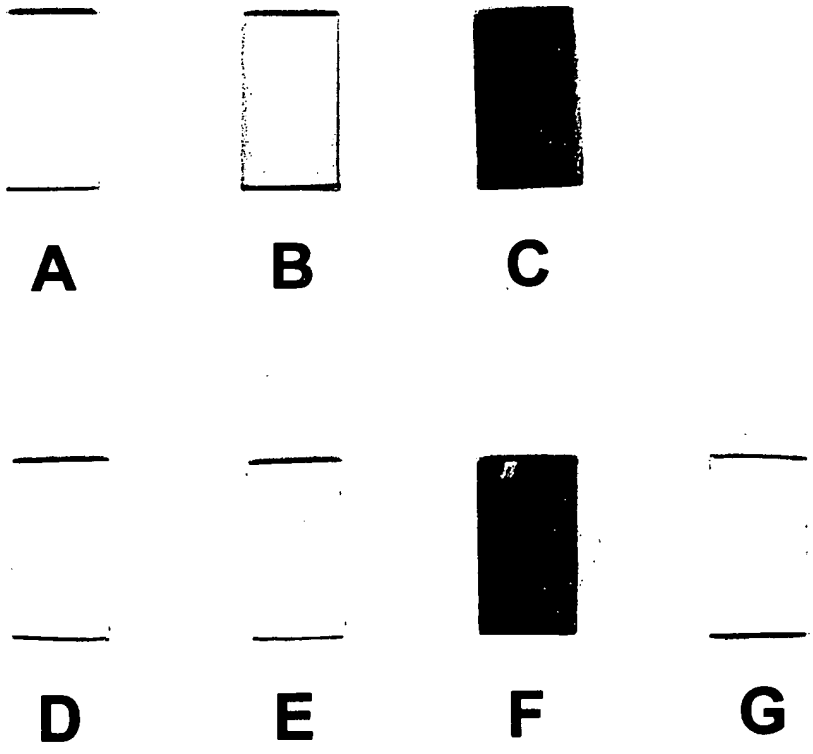


FIG. 34

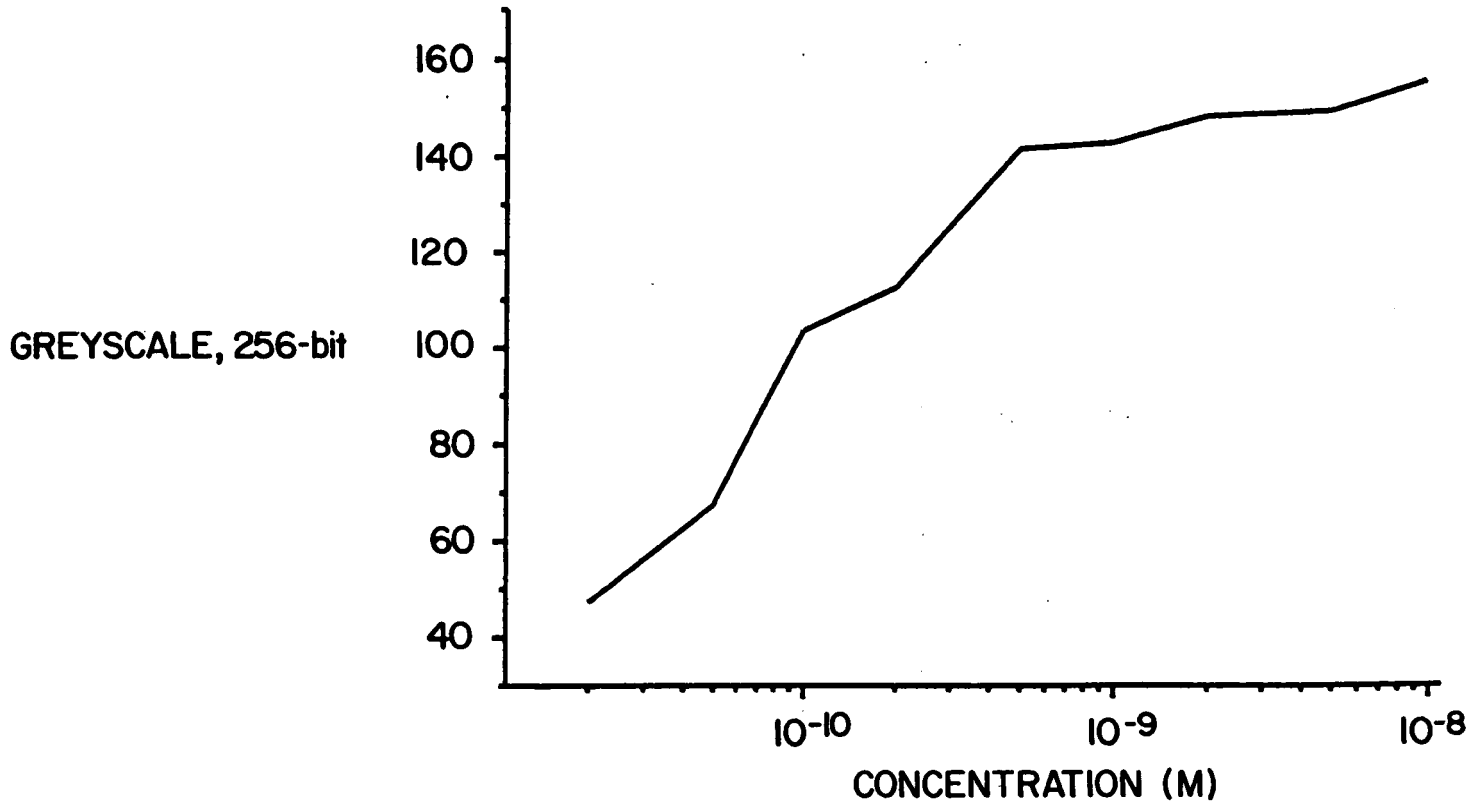


FIG.35A

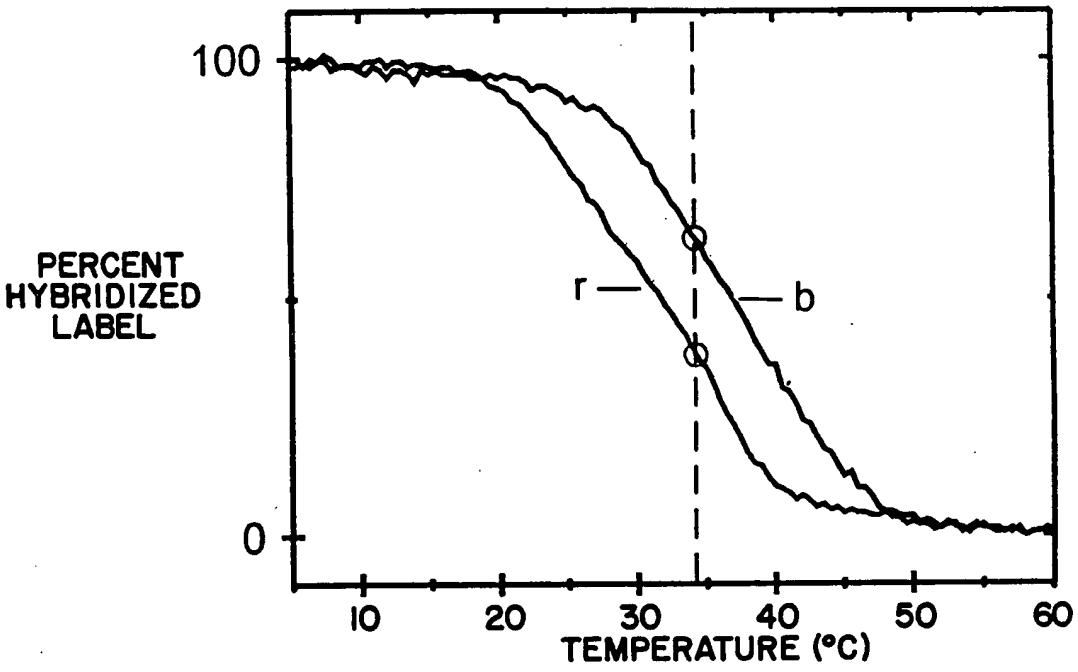


FIG.35B

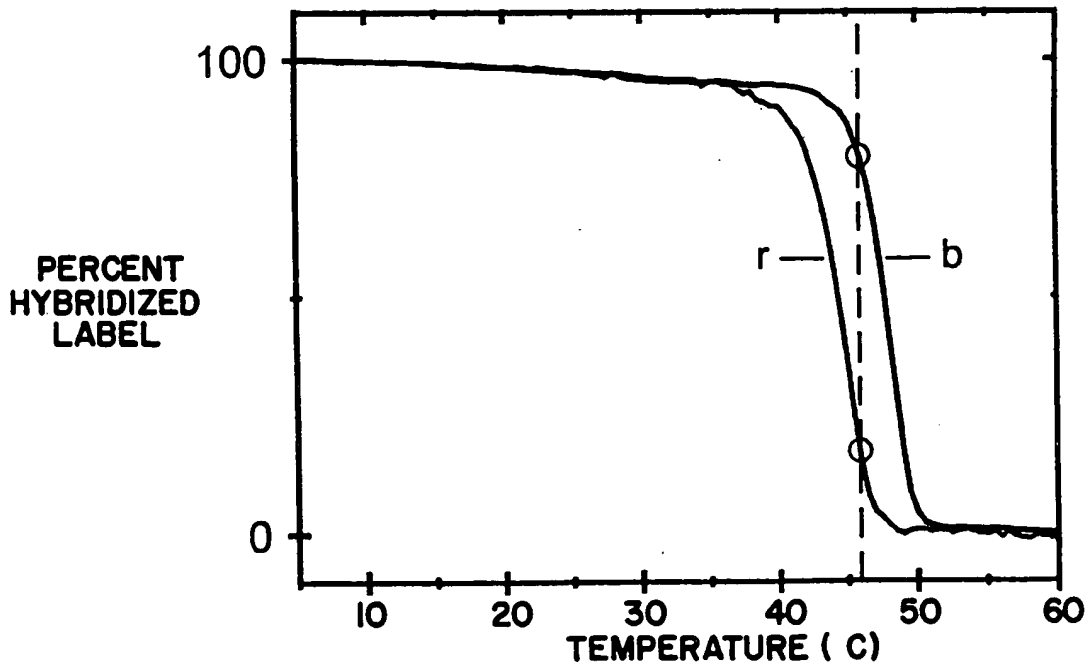


FIG. 36A

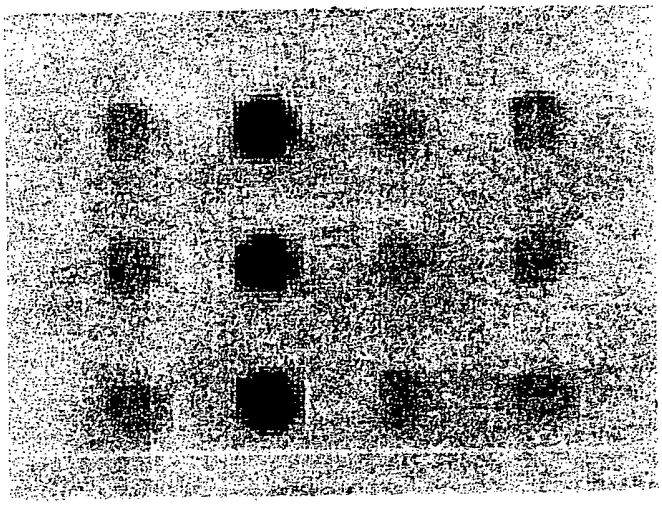
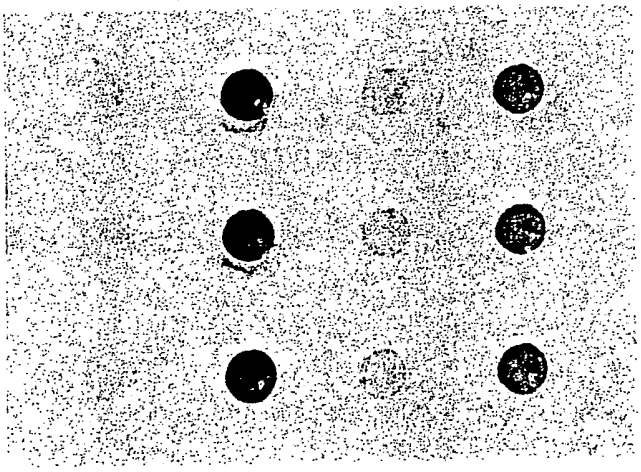


FIG. 36B



C A T G

FIG.37A

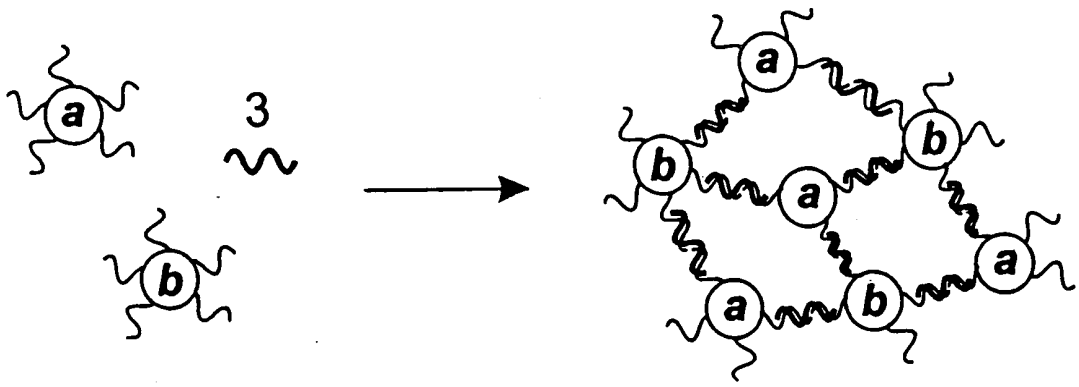


FIG.37B

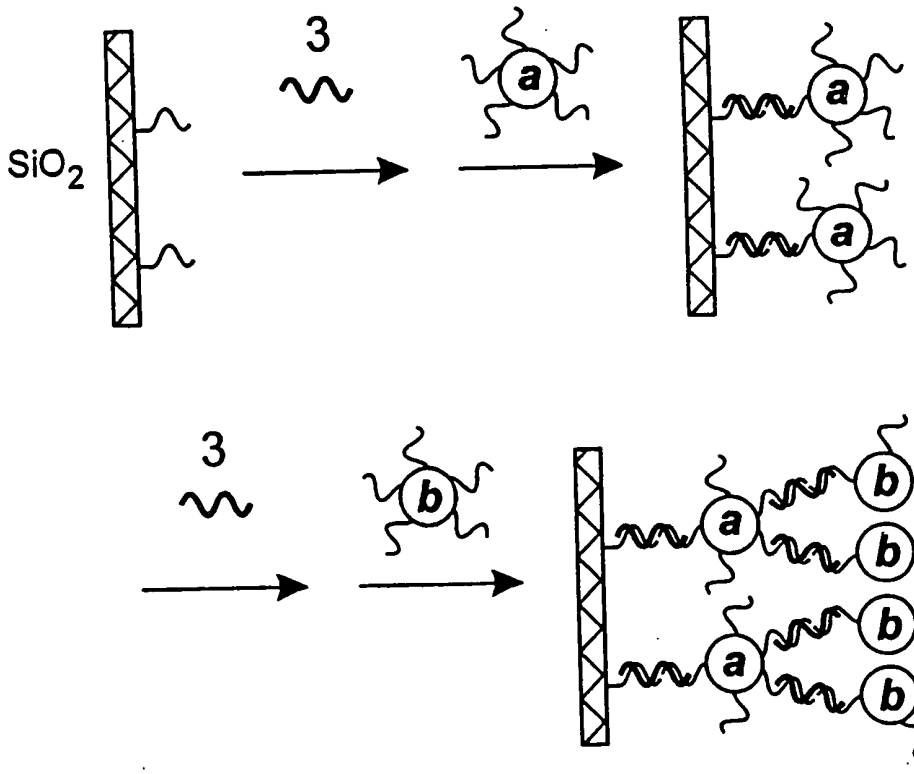


FIG. 38A

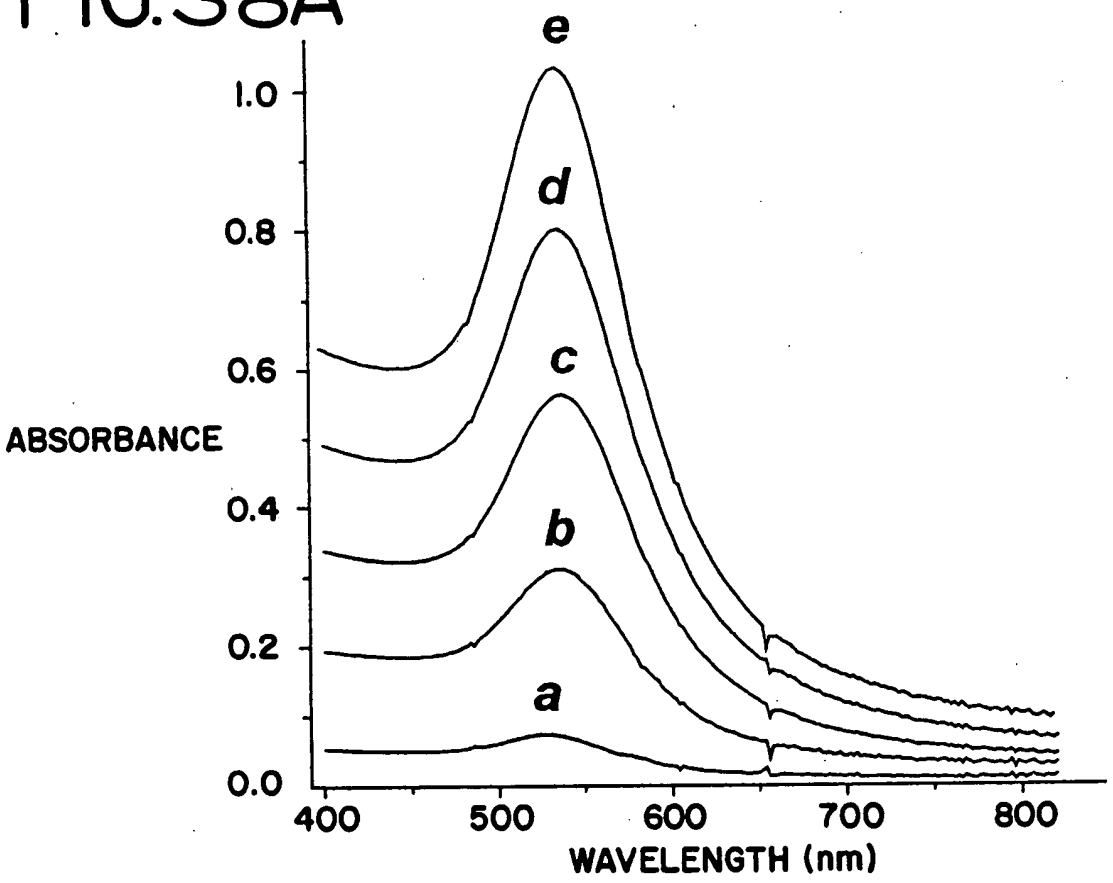


FIG. 38B

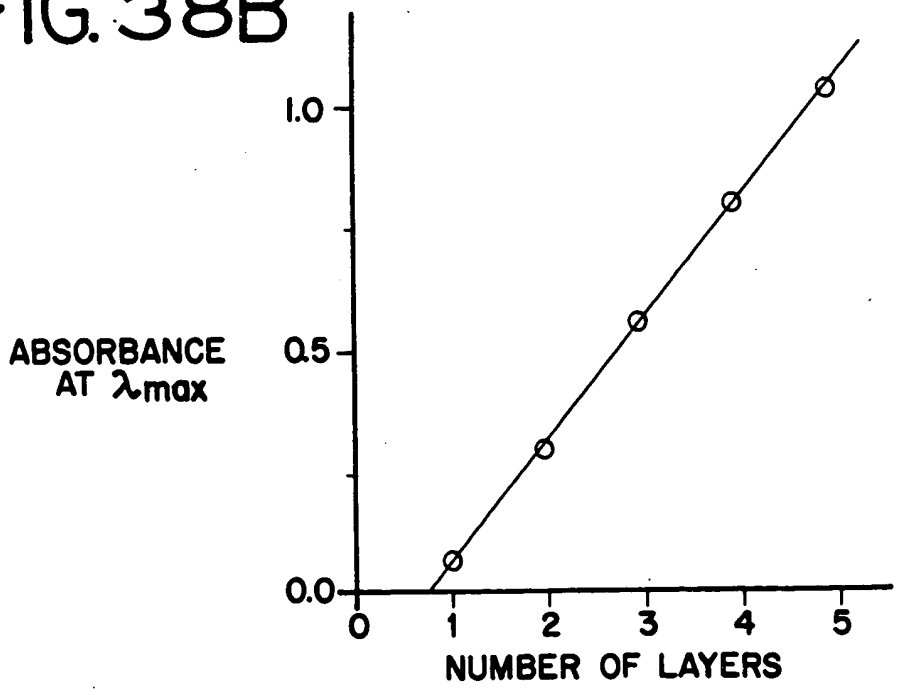


FIG. 39A

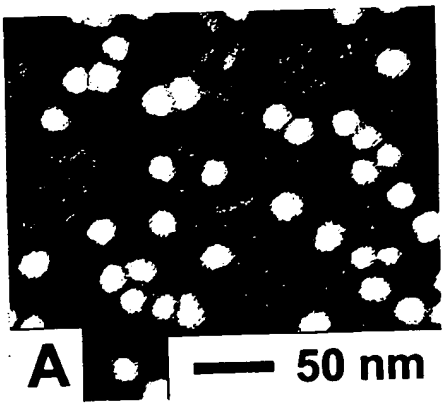


FIG. 39B

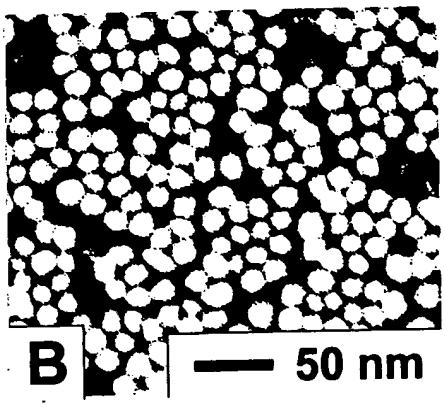


FIG.39C

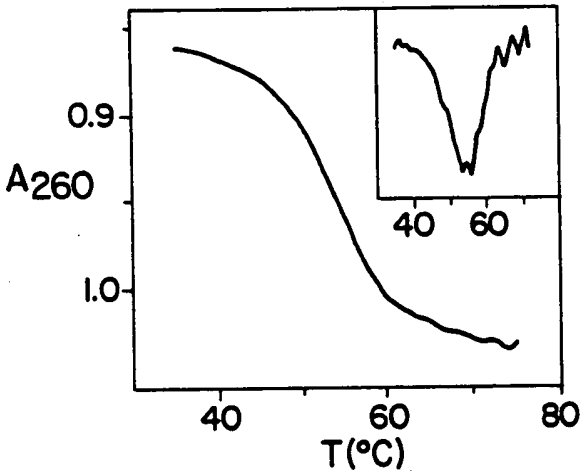


FIG.39D

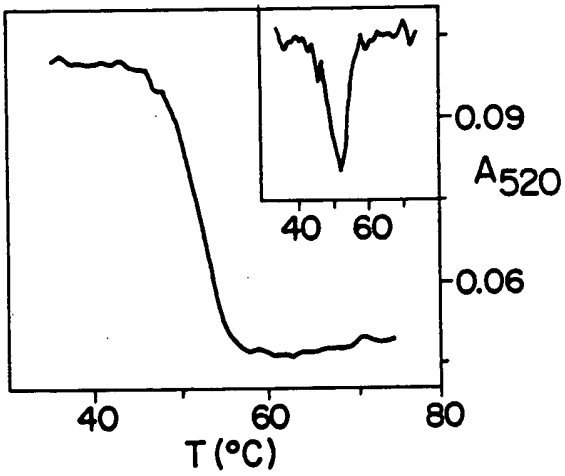


FIG.39E

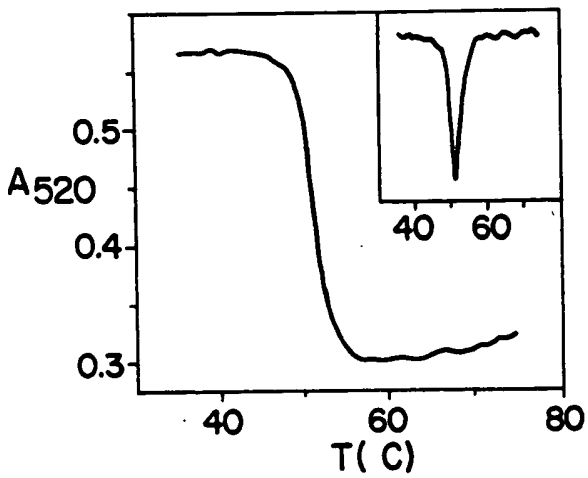


FIG.39F

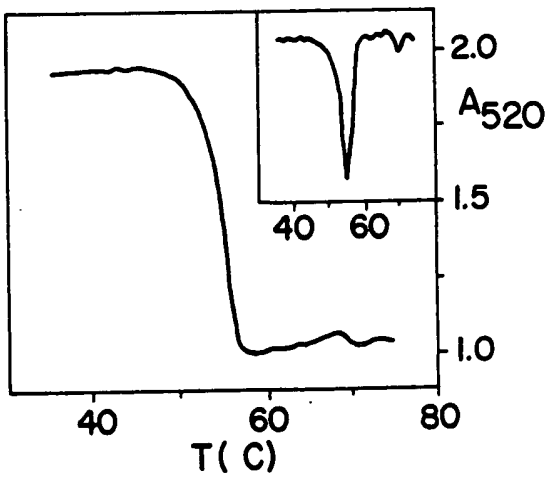


FIG. 40

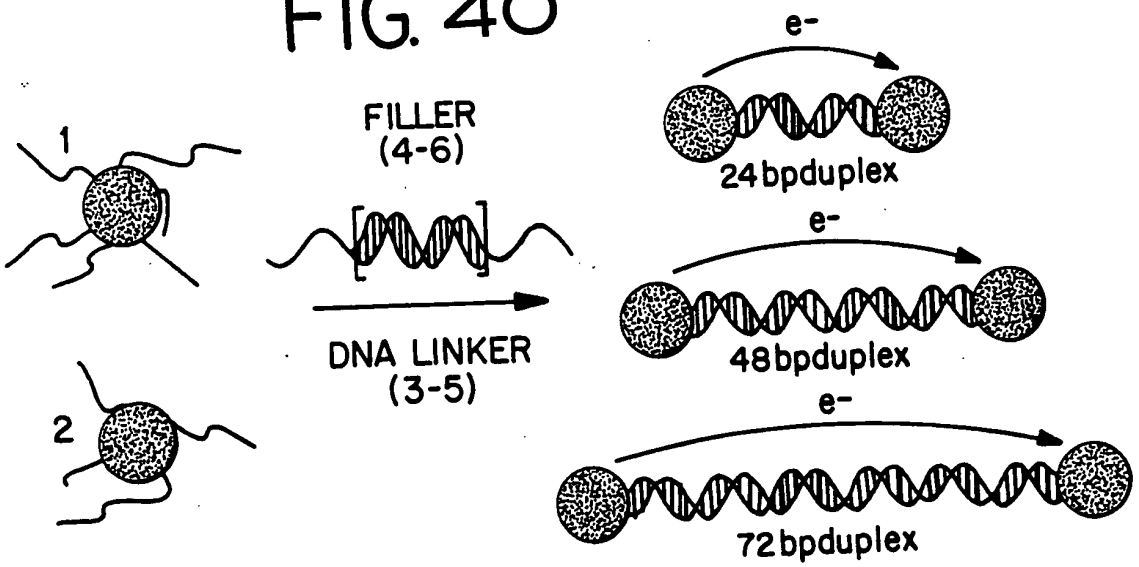

1
2
FILLER
(4-6)
DNA LINKER
(3-5)
e-
24bpduplex
e-
48bpduplex
e-
72bpduplex

FIG. 41

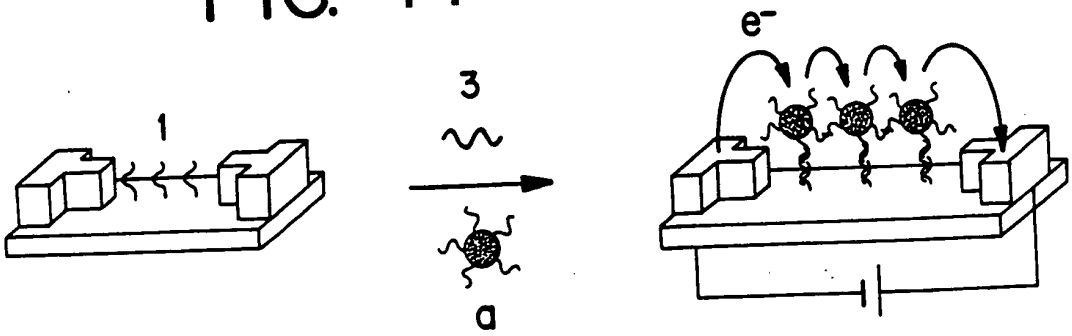
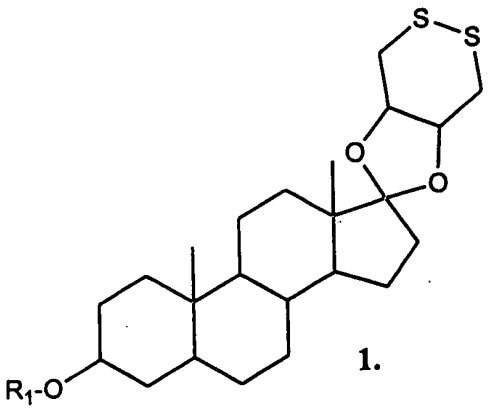

1
3
a
e-

FIG. 42



1.

II $HS-(CH_2)_6OR_1$

III $S-(CH_2)_6OR_1$ / $S-(CH_2)_6OH$

R_1

a = H
b = $(iPr)_2NP(OCH_2CH_2CN)$-
c1 = 5'p(A_{20})-TATCGTTCCATCAGCT [SEQ ID NO: 65]
c2 = 5'-p(A_{20})-TTGATCTTCCGTTCT [SEQ ID NO: 66]
Target I = 79-mer oligonucleotide with target region:
3'-.....ATAGCAAGGTAGTCGAGCAACTAGAAAGGCAAGA.....5'
[SEQ ID NO: 67]

FIG. 43

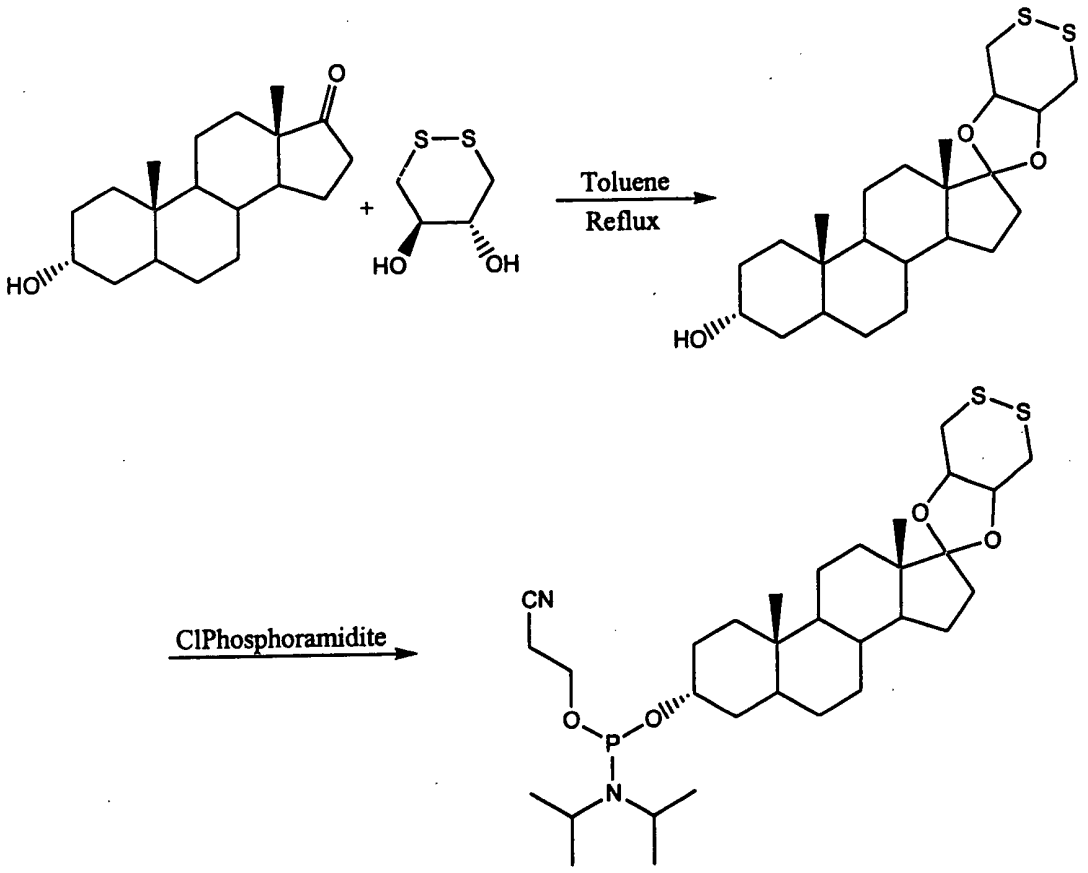
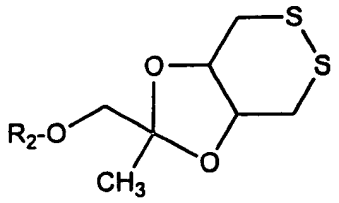

HO
O
S—S
HO
OH
+
Toluene
Reflux
HO
S
S
O
O
ClPhosphoramidite
CN
O
P
O
N

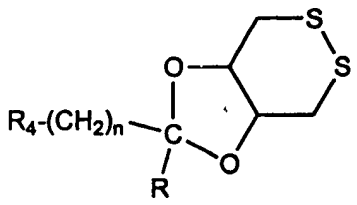
FIG. 44



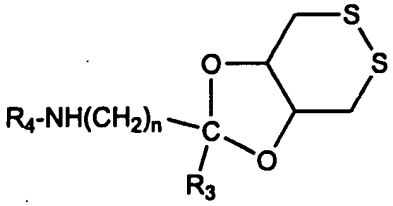
2.

R_2

a = H
b = $(iPr)_2NP(OCH_2CH_2CN)$-
c1 = 5'-p(A_{20})-GCAGACCTCA [SEQ ID NO: 68]
c2 = 5'-p(A_{20})-CCTATGTGTCG [SEQ ID NO: 69]
D = 5'-p(A_{20}) [SEQ ID NO: 70]
Target I = 63-mer oligonucleotide with target region:
3'-.....CGTCTGGAGTGGATACACAGC.....5'
[SEQ ID NO: 71]



3.



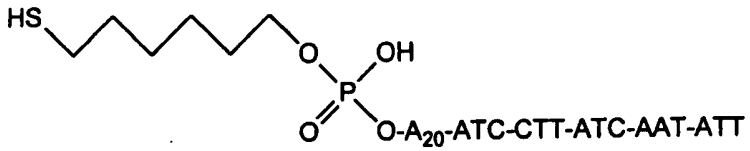
4.

R_3 = hydrogen, an alkyl group, an aryl group, or a substituted alkyl or aryl group

R_4 = an attached oligonucleotide or modified oligonucleotide

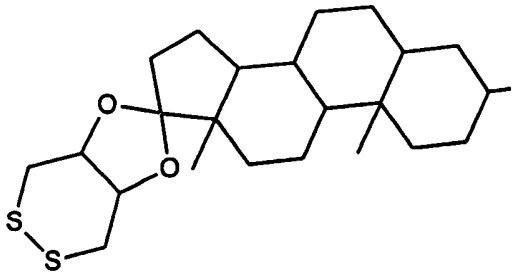
FIG. 45

5.



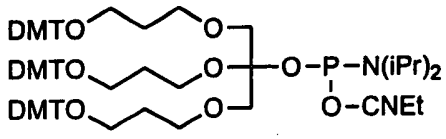
[SEQ ID NO: 72]

6.

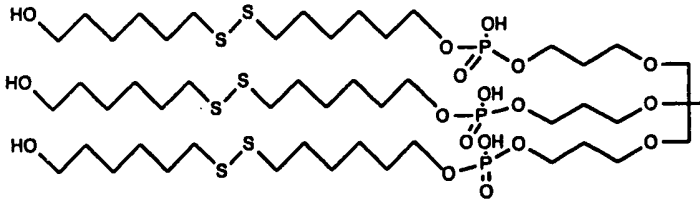


[SEQ ID NO: 72]

7.

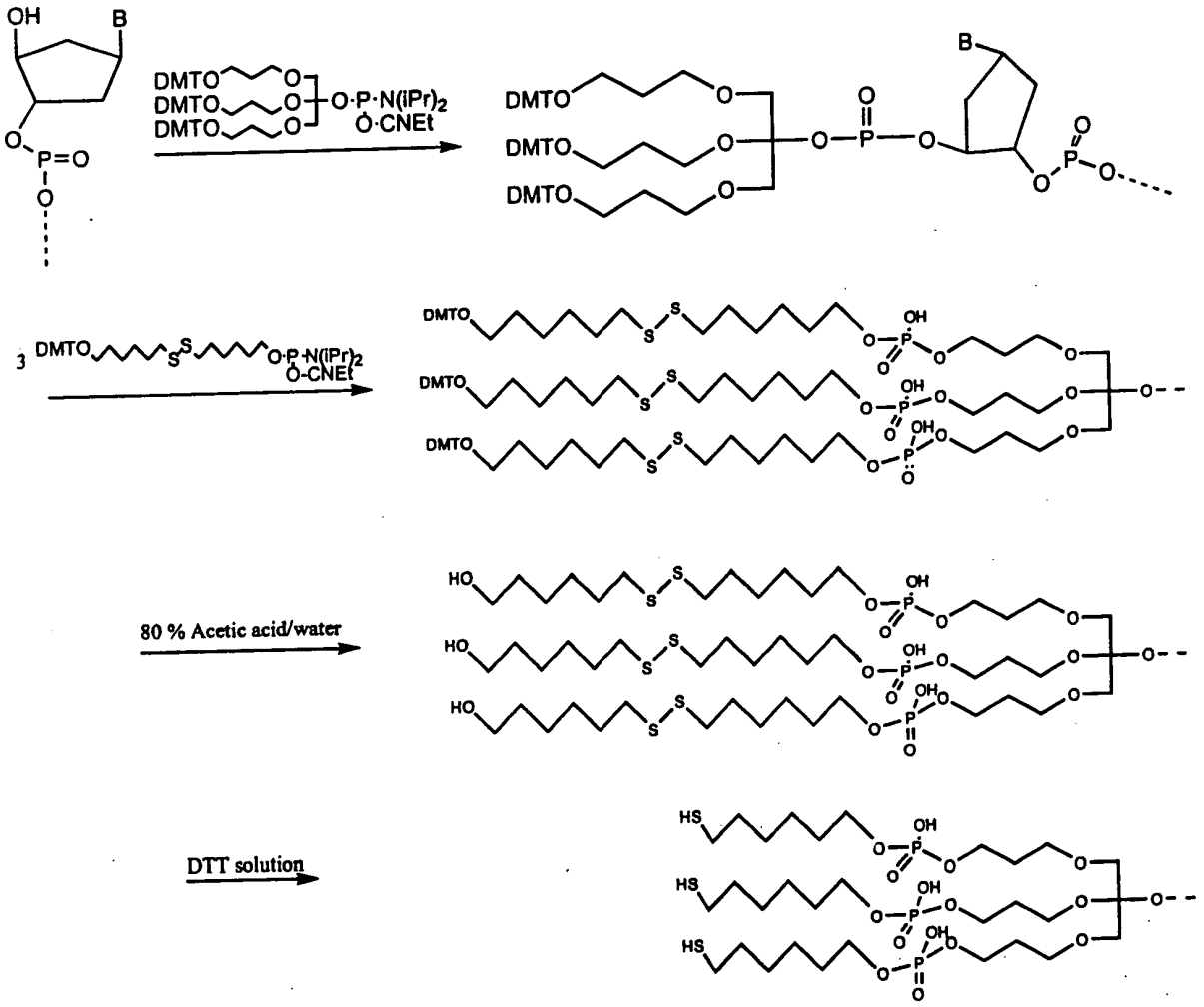


8.



[SEQ ID NO: 72]

FIG. 46


OH
B
DMTO
DMTO
DMTO
O·P·N(iPr)2
O·CNEt
P=O
O
B
DMTO
DMTO
DMTO
3 DMTO
S
S
O·P·N(iPr)2
O-CNEt
DMTO
DMTO
DMTO
OH
80 % Acetic acid/water
HO
HO
HO
DTT solution
HS
HS
HS

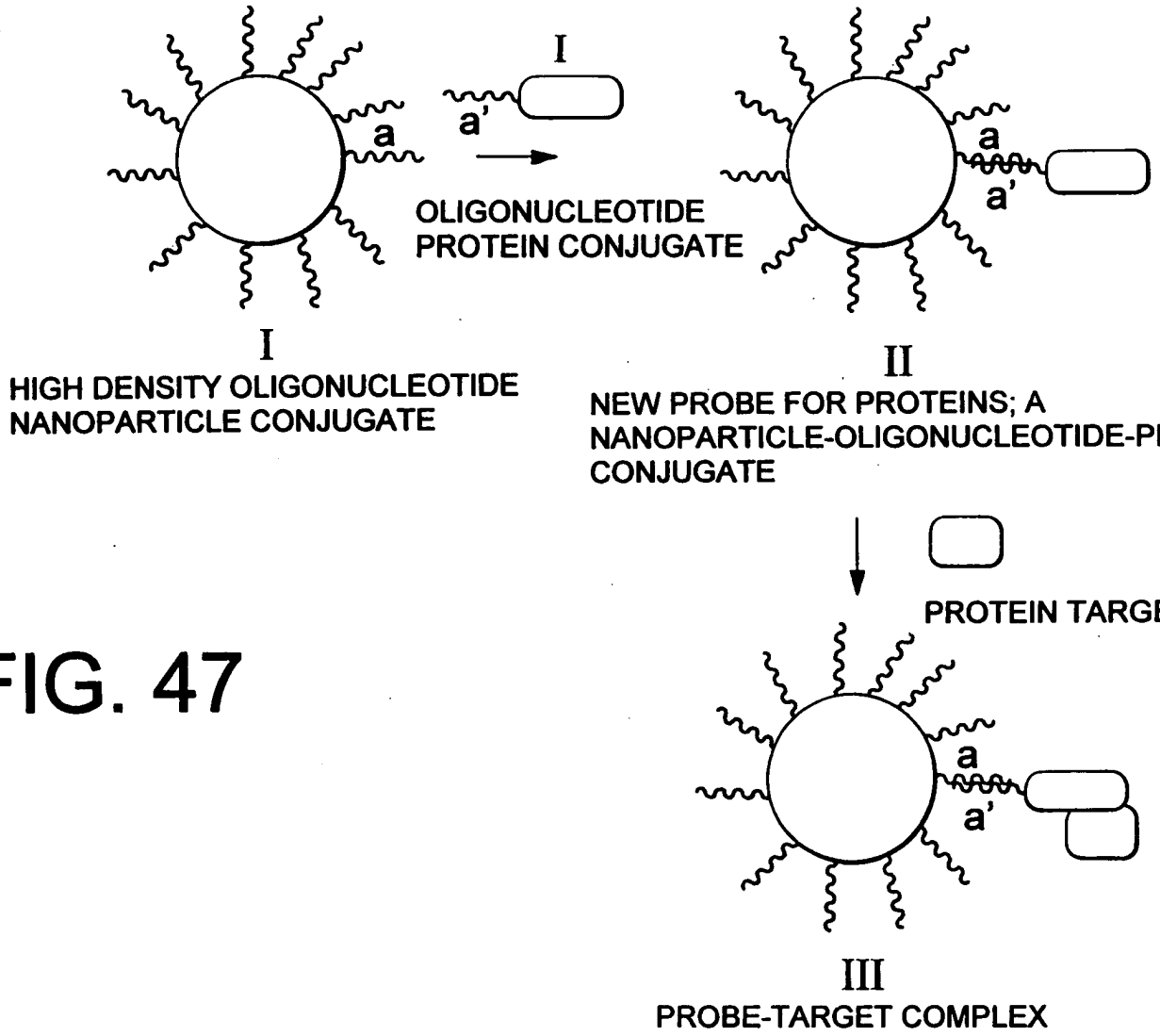
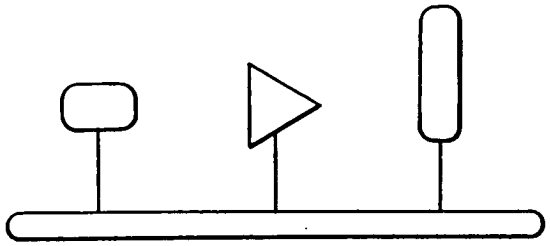
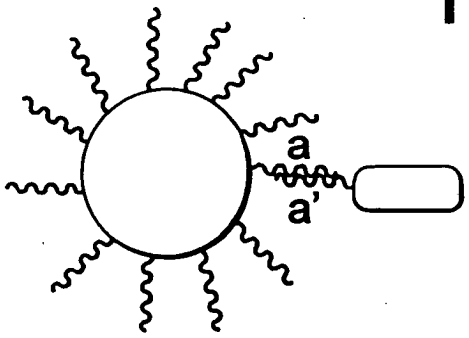

I
a'
a
OLIGONUCLEOTIDE
PROTEIN CONJUGATE
a
a'
I
HIGH DENSITY OLIGONUCLEOTIDE
NANOPARTICLE CONJUGATE
II
NEW PROBE FOR PROTEINS; A
NANOPARTICLE-OLIGONUCLEOTIDE-PROTEIN
CONJUGATE
PROTEIN TARGET
a
a'
III
PROBE-TARGET COMPLEX

FIG. 47

FIG. 48



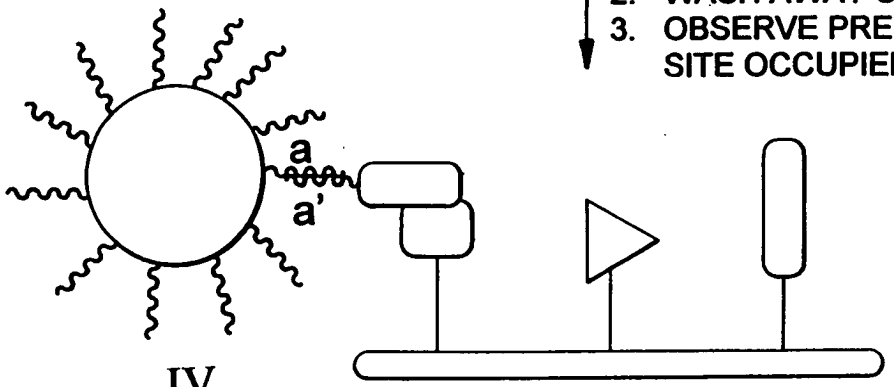
GLASS PLATE WITH THREE DIFFERENT PROTEINS IMMOBLIZED ON THE SURFACE, ONE OF WHICH BINDS TO THE PROTEIN IN PROBE II



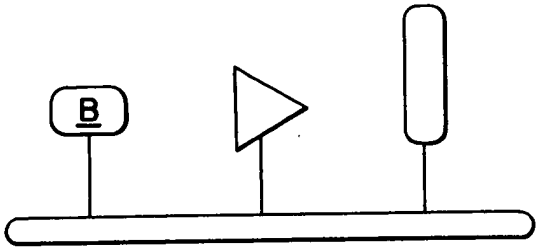
II

NEW PROBE FOR PROTEINS; A NANOPARTICLE-OLIGONUCLEOTIDE-PROTEIN CONJUGATE

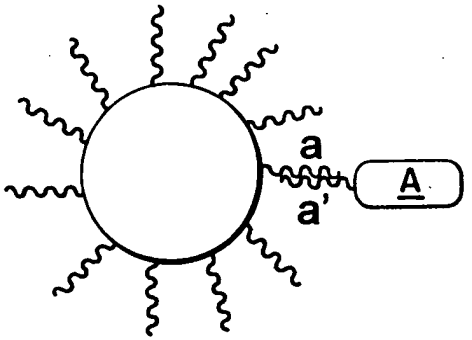
1. EXPOSE PLATE TO THE PROBE SOLUTION
2. WASH AWAY UNBOUND NANOPARTICLE PROBE
3. OBSERVE PRESENCE OF BOUND NANOPARTICLES AT SITE OCCUPIED BY THE FIRST PROTEIN IN THE SERIES.



IV

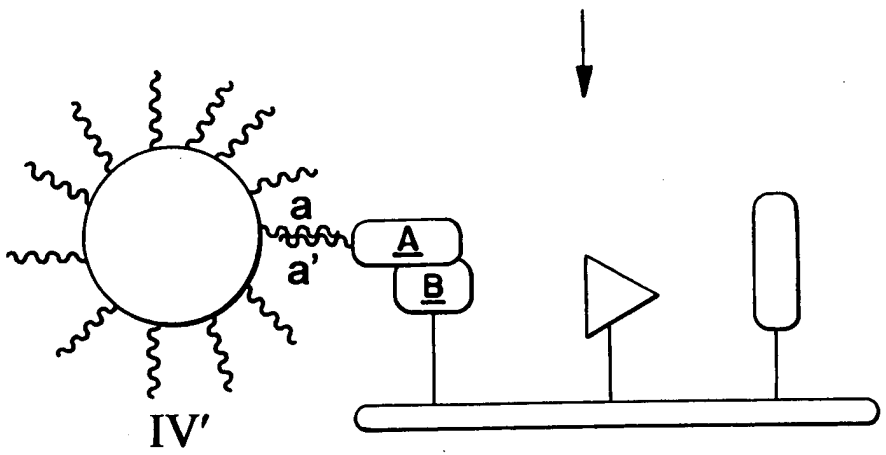


GLASS PLATE WITH THREE DIFFERENT SUBSTANCES IMMOBILIZED ON THE SURFACE, ONE OF WHICH (B) BINDS TO THE RECEPTOR UNIT (A) IN II'.



II'

NANOPARTICLE-OLIGONUCLEOTIDE-RECEPTOR



IV'

FIG. 49

FIG. 50A

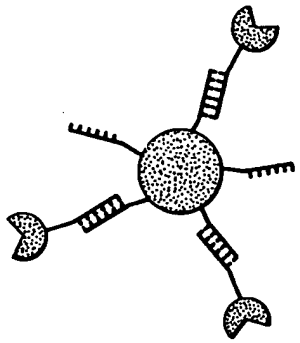


FIG. 51A

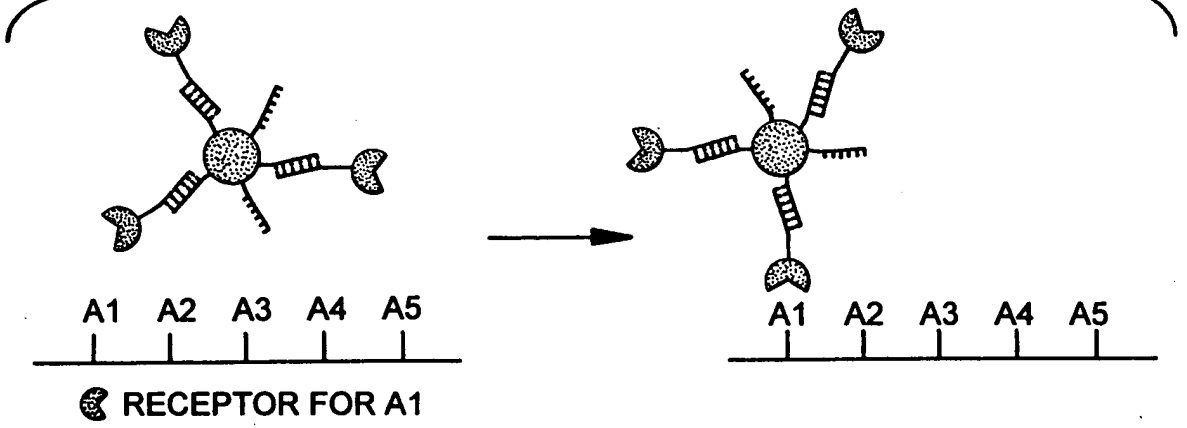


FIG. 50B

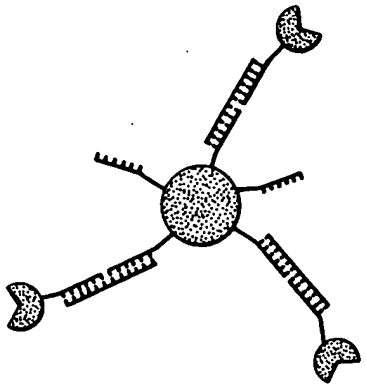


FIG. 51B

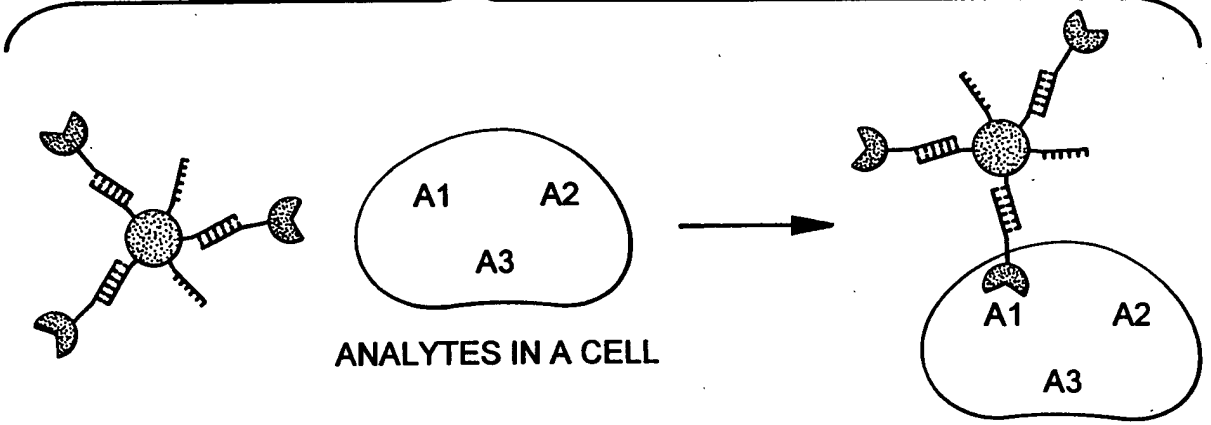


FIG. 52A

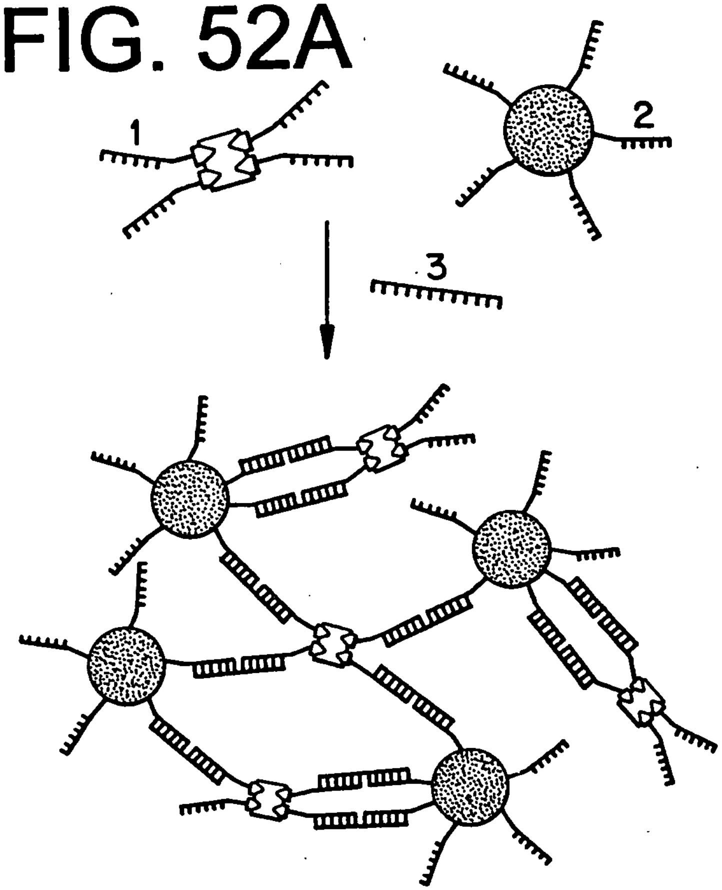
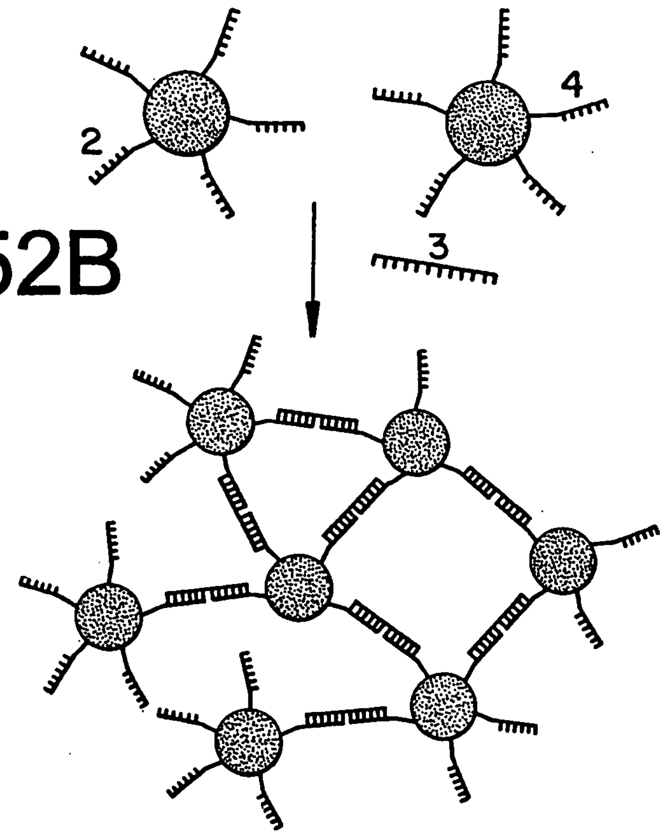


FIG. 52B



1 3' biotin-TEG-A_{10}-ATG CTC AAC TCT 5' [SEQ. ID NO. 73]

2 5' SH$(CH_2)_6$-A_{10}-CGC ATT CAG GAT 3' [SEQ. ID NO. 74]

3 5' TAC GAG TTG AGA ATC CTG AAT GCG 3' [SEQ. ID NO. 75]

13 nm Au NANOPARTICLES STREPTAVIDIN

2 5' SH$(CH_2)_6$-A_{10}-CGC ATT CAG GAT 3'

3 5' TAC GAG TTG AGA ATC CTG AAT GCG 3'

4 3' SH$(CH_2)_3$-A_{10}-ATG CTC AAC TCT 5'

13 nm Au NANOPARTICLES

FIG. 52C

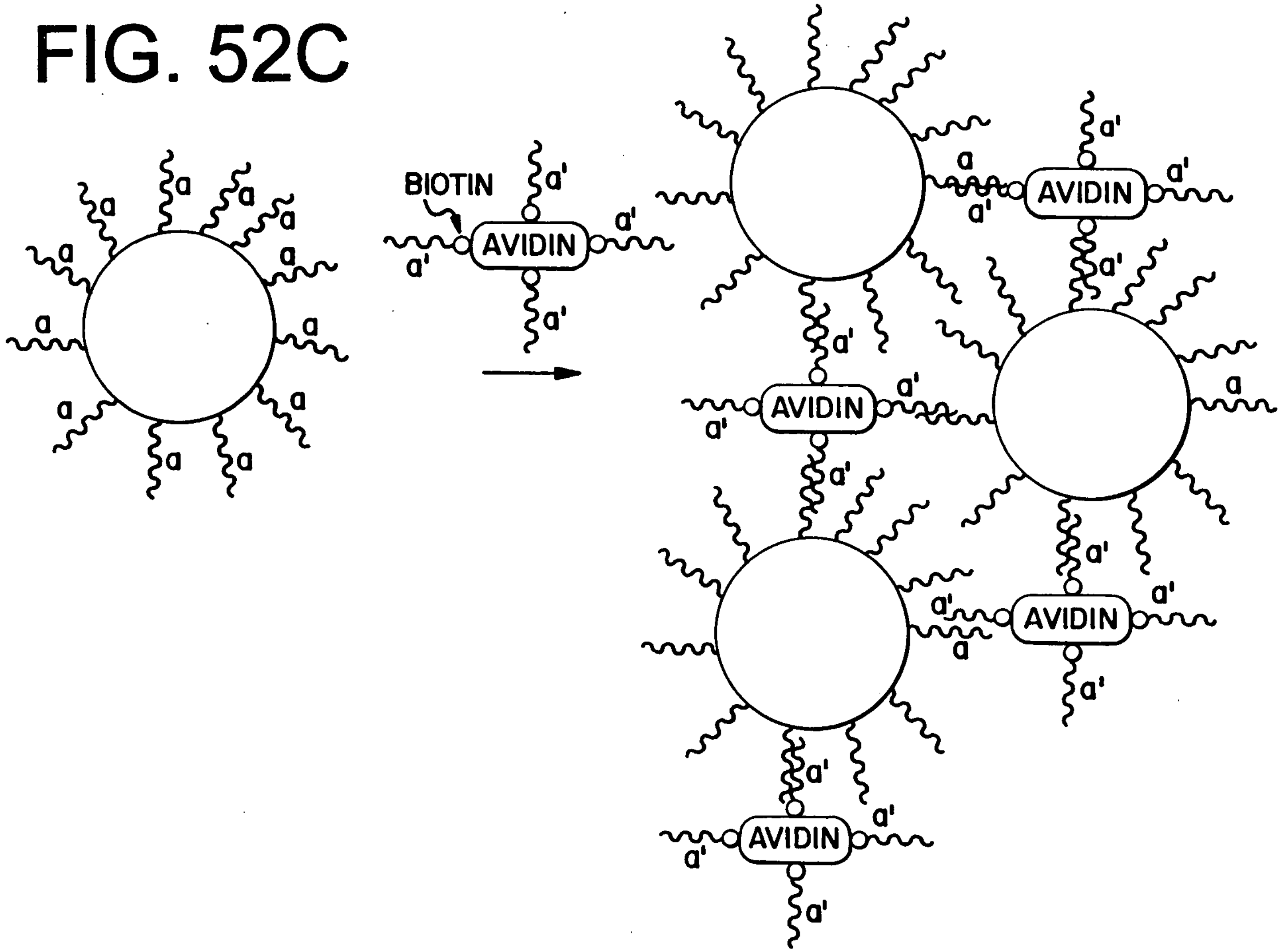
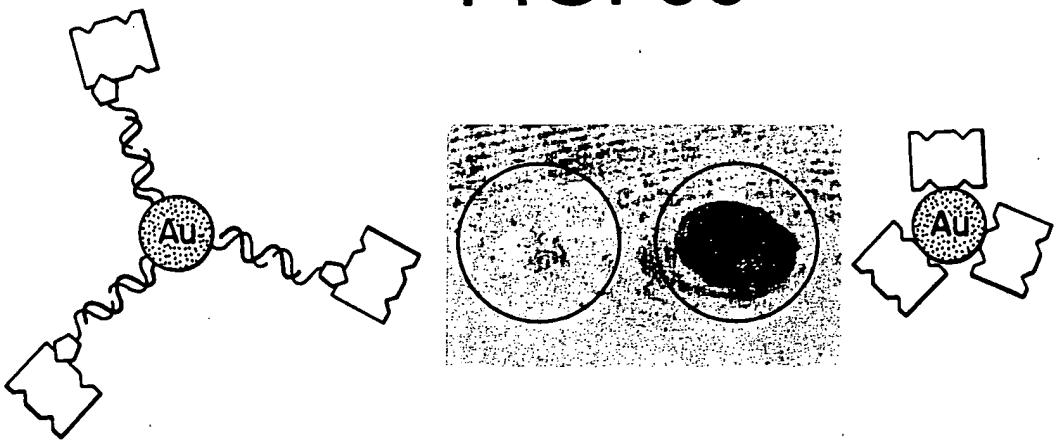


FIG. 53



Au COLLOID / DNA / STREPTAVIDIN CONJUGATE vs. Au COLLOID / STREPTAVIDIN CONJUGATE

FIG. 54

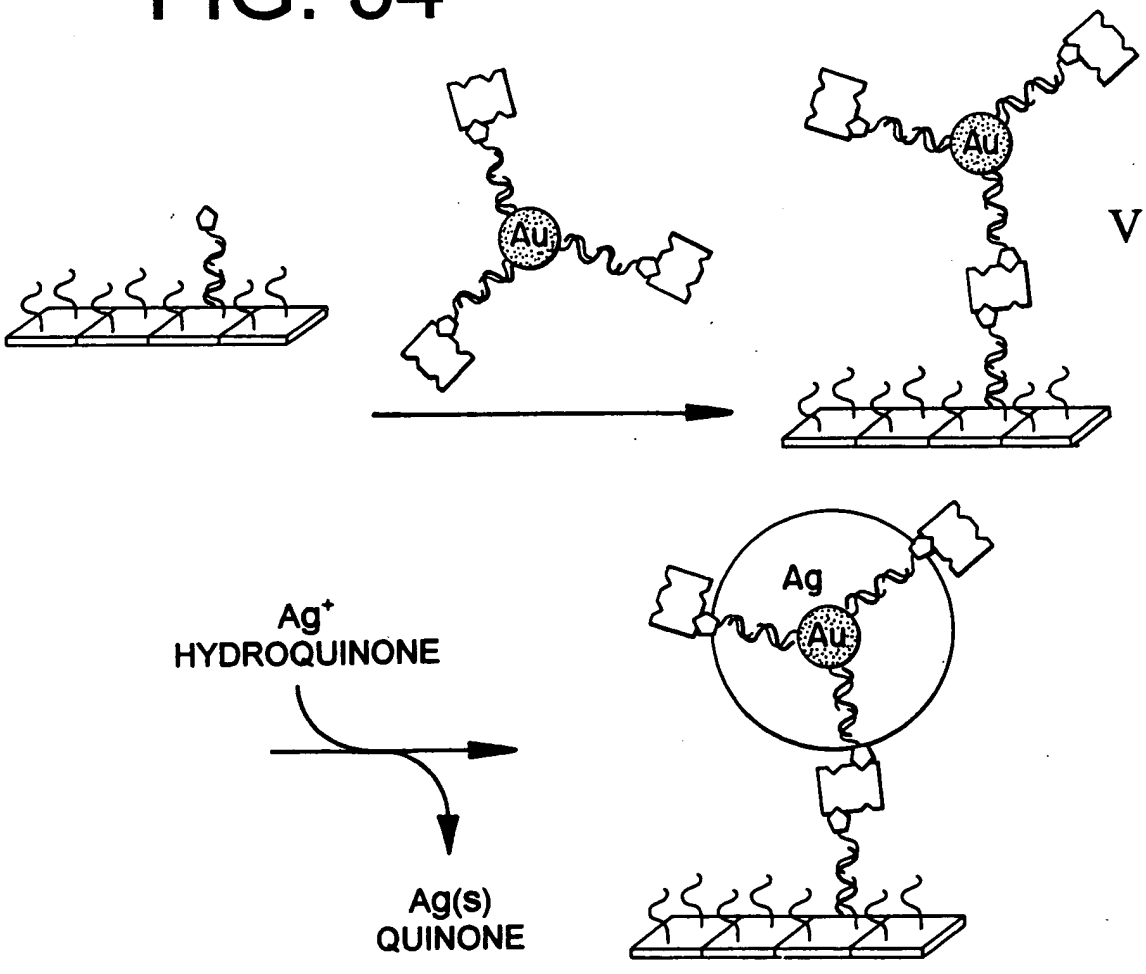


FIG. 55

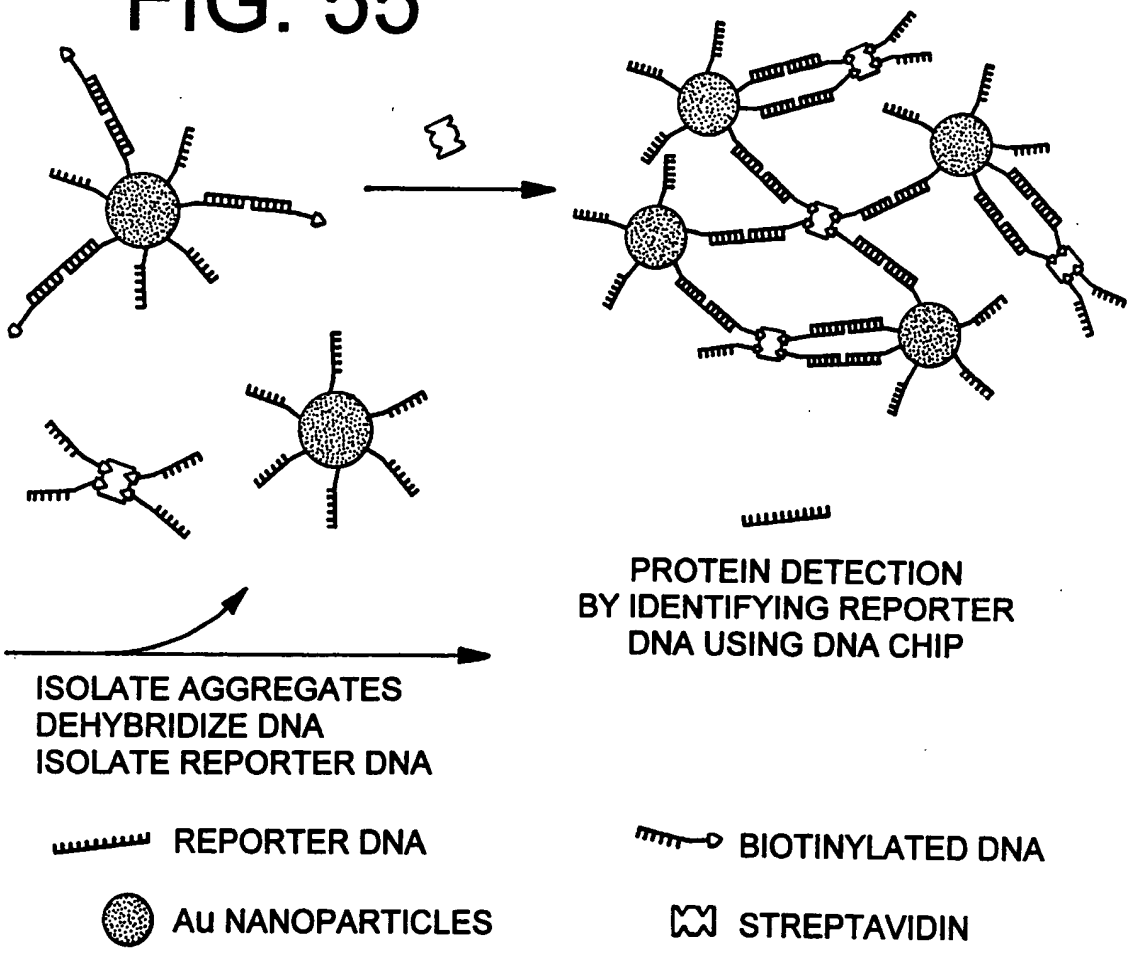
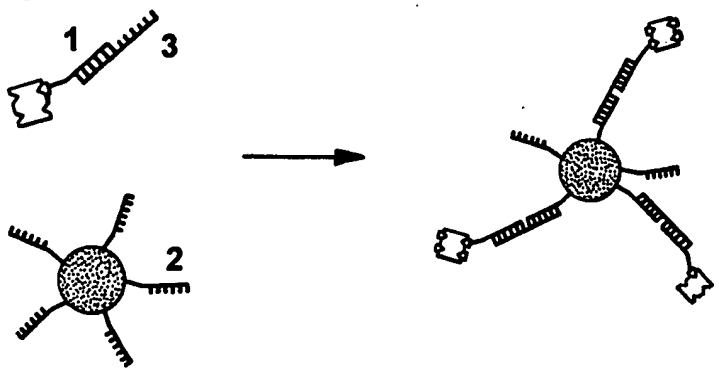


FIG. 56



1 3' BIOTIN-TEG-A_{10}-ATG CTC AAC TCT 5' [SEQ.ID NO: 73]

2 5' $SH(CH_2)_6$-A_{10}-CGC ATT CAG GAT 3' [SEQ. ID NO: 74]

3 5' TAC GAG TTG AGA ATC CTG AAT GCG 3' [SEQ. ID NO: 75]

13nm Au NANOPARTICLES

STREPTAVIDIN

LINKER DNA

BIOTINYLATED DNA

FIG. 57A

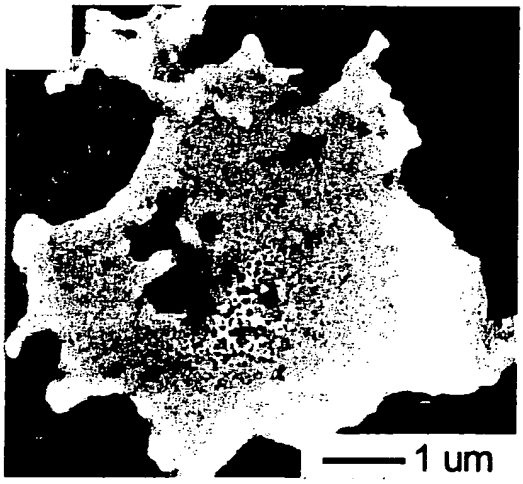


FIG. 57B

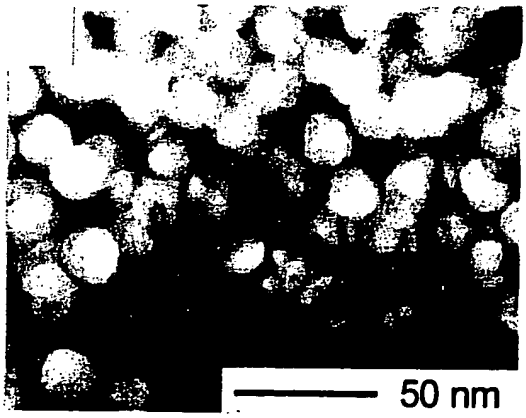


FIG. 58A

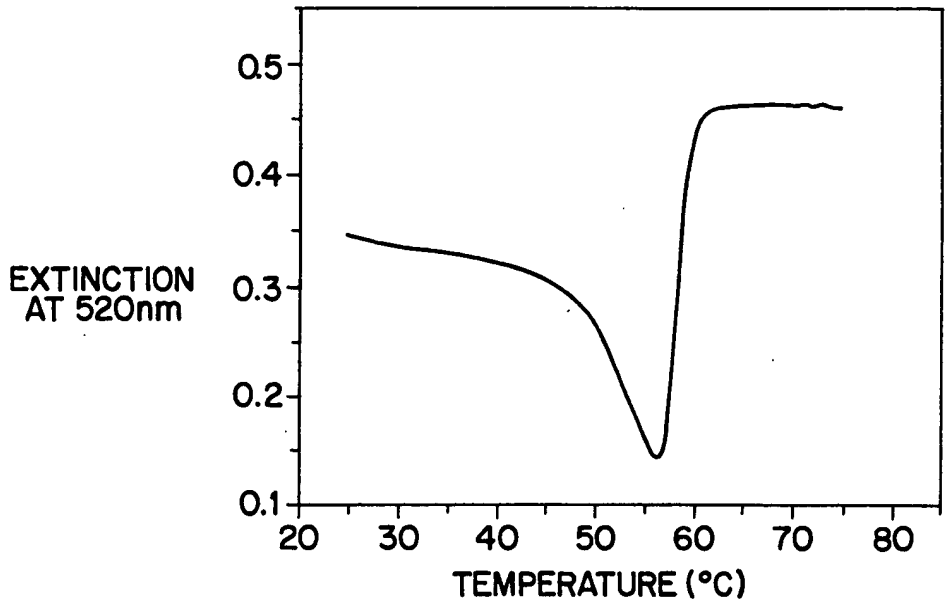


FIG. 58B

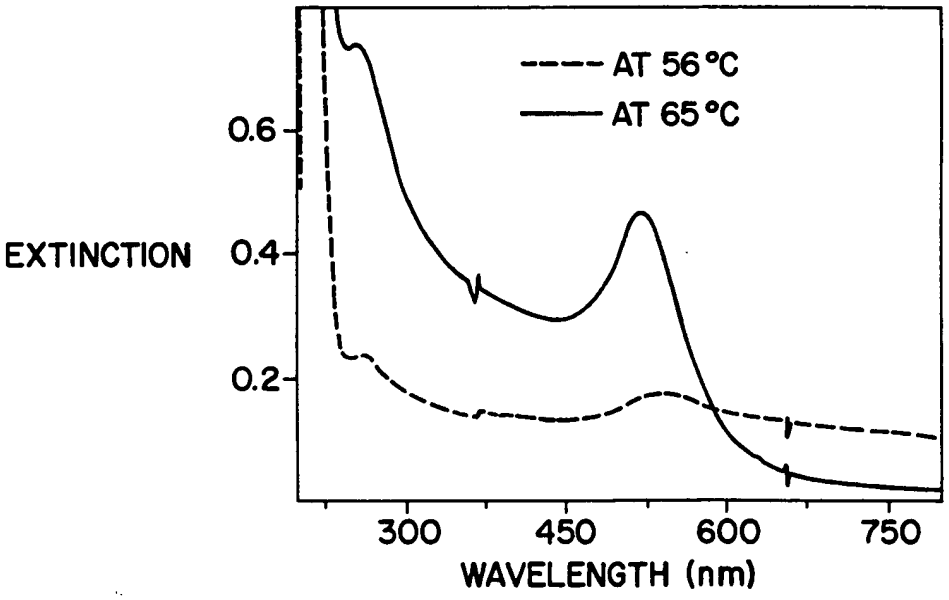


FIG. 59

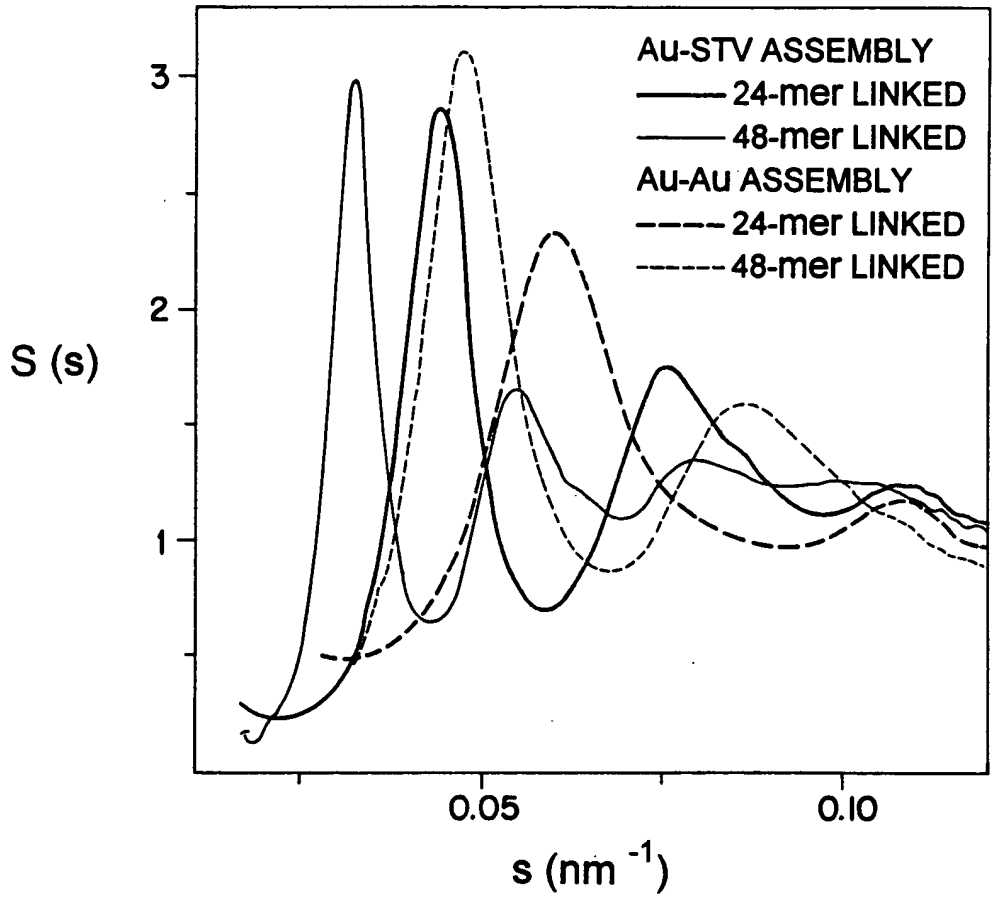

Au-STV ASSEMBLY
24-mer LINKED
48-mer LINKED
Au-Au ASSEMBLY
24-mer LINKED
48-mer LINKED
S (s)
3
2
1
0.05
0.10
s (nm -1)

FIG. 60

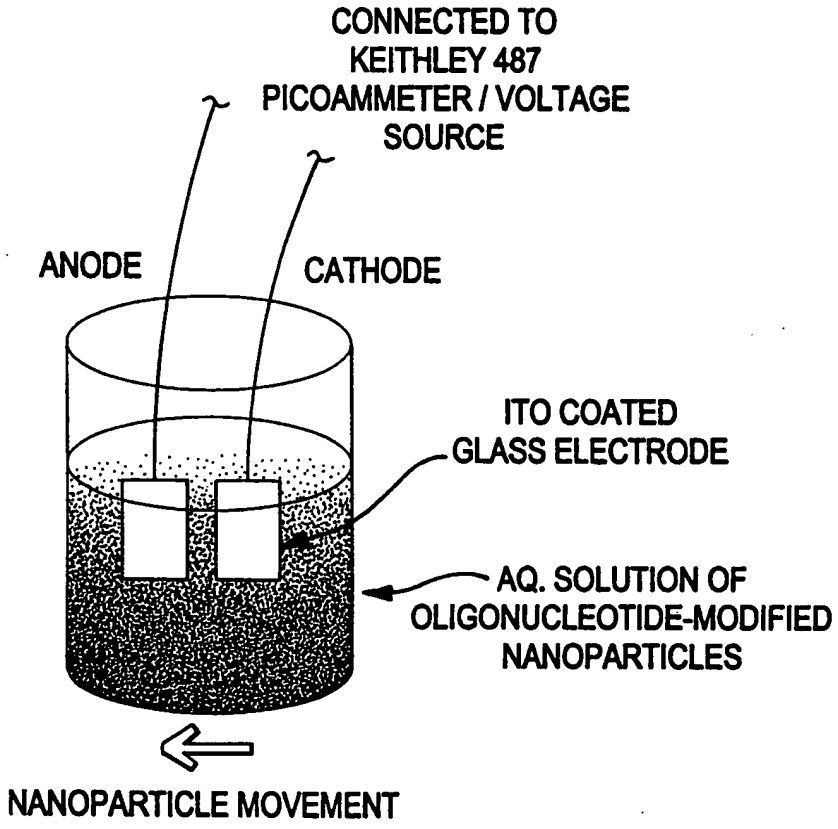
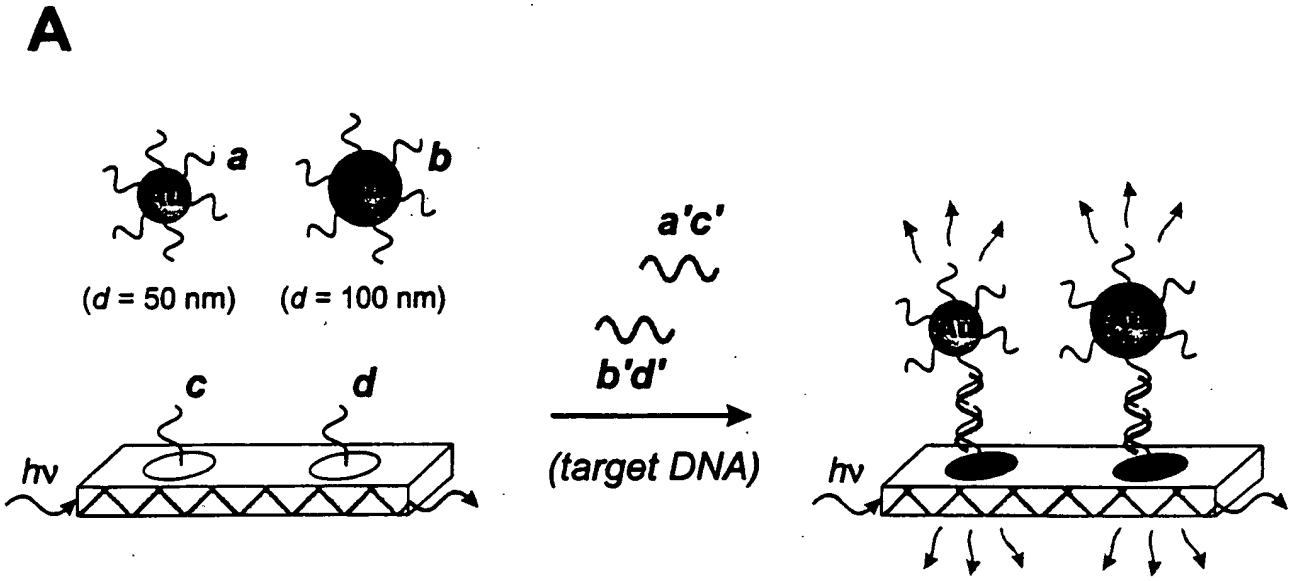
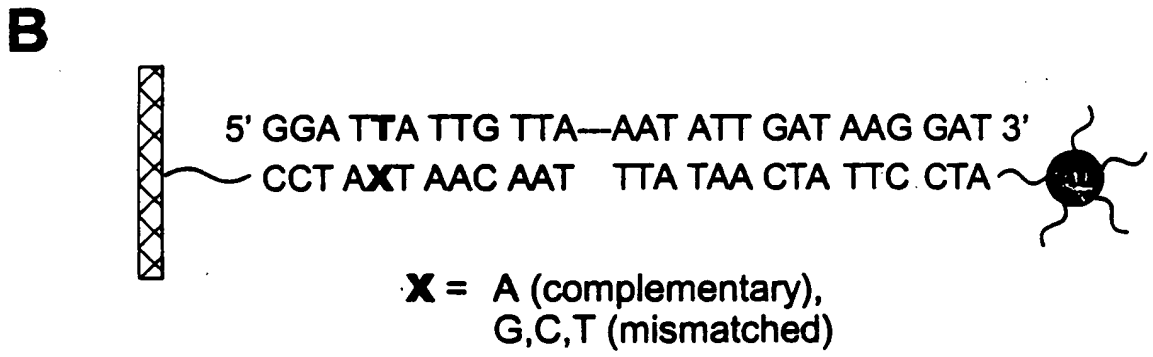

CONNECTED TO
KEITHLEY 487
PICOAMMETER / VOLTAGE
SOURCE
ANODE
CATHODE
ITO COATED
GLASS ELECTRODE
AQ. SOLUTION OF
OLIGONUCLEOTIDE-MODIFIED
NANOPARTICLES
NANOPARTICLE MOVEMENT

Figure 61


A
a
b
(d = 50 nm)
(d = 100 nm)
c
d
hν
a'c'
b'd'
(target DNA)
hν


B
5' GGA TTA TTG TTA—AAT ATT GAT AAG GAT 3'
CCT AXT AAC AAT TTA TAA CTA TTC CTA
X = A (complementary),
G,C,T (mismatched)

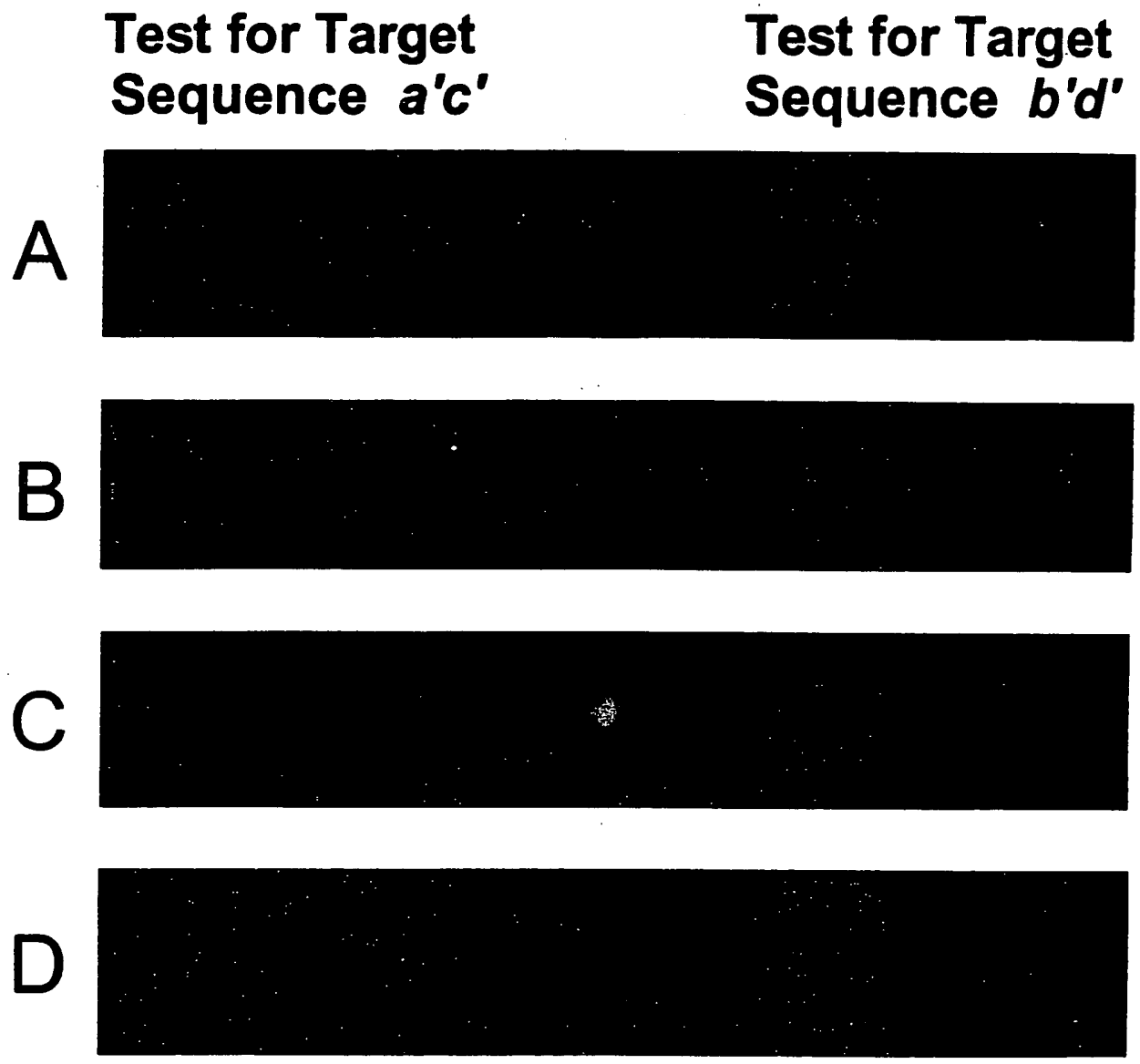
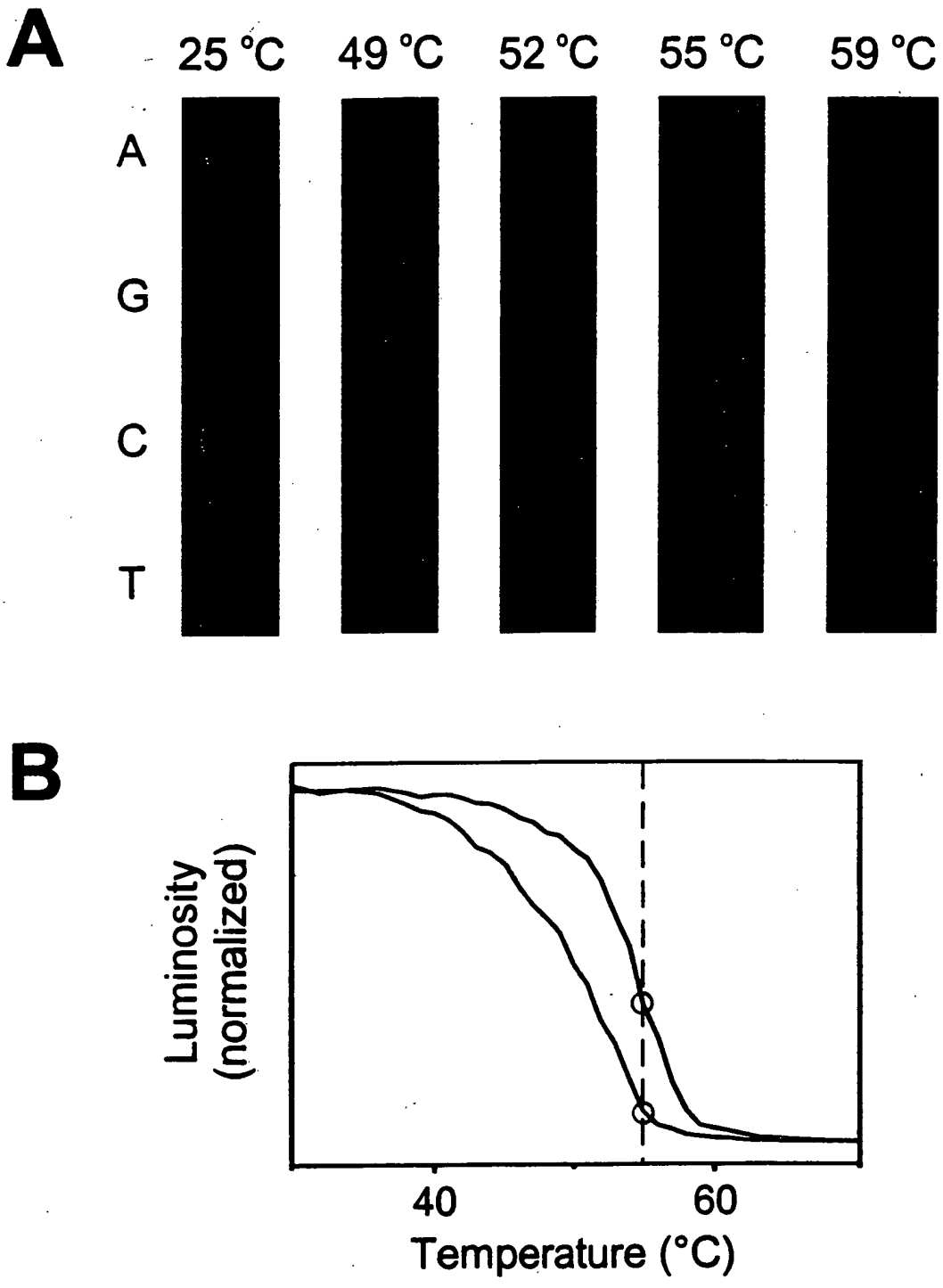


Figure 6Y

G. Lu, T. A. Taton and C. A. Mirkin



G. Lu, T. A. Taton and C. A. Mirkin

Figure 63

Figure 64

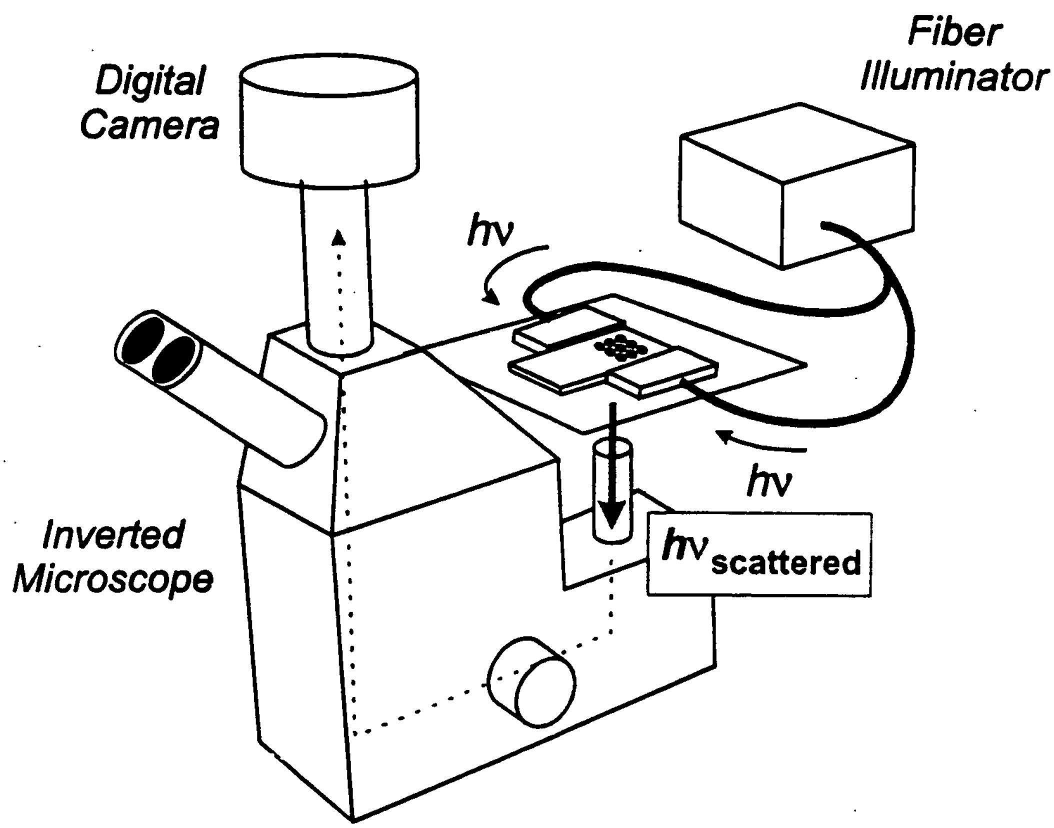
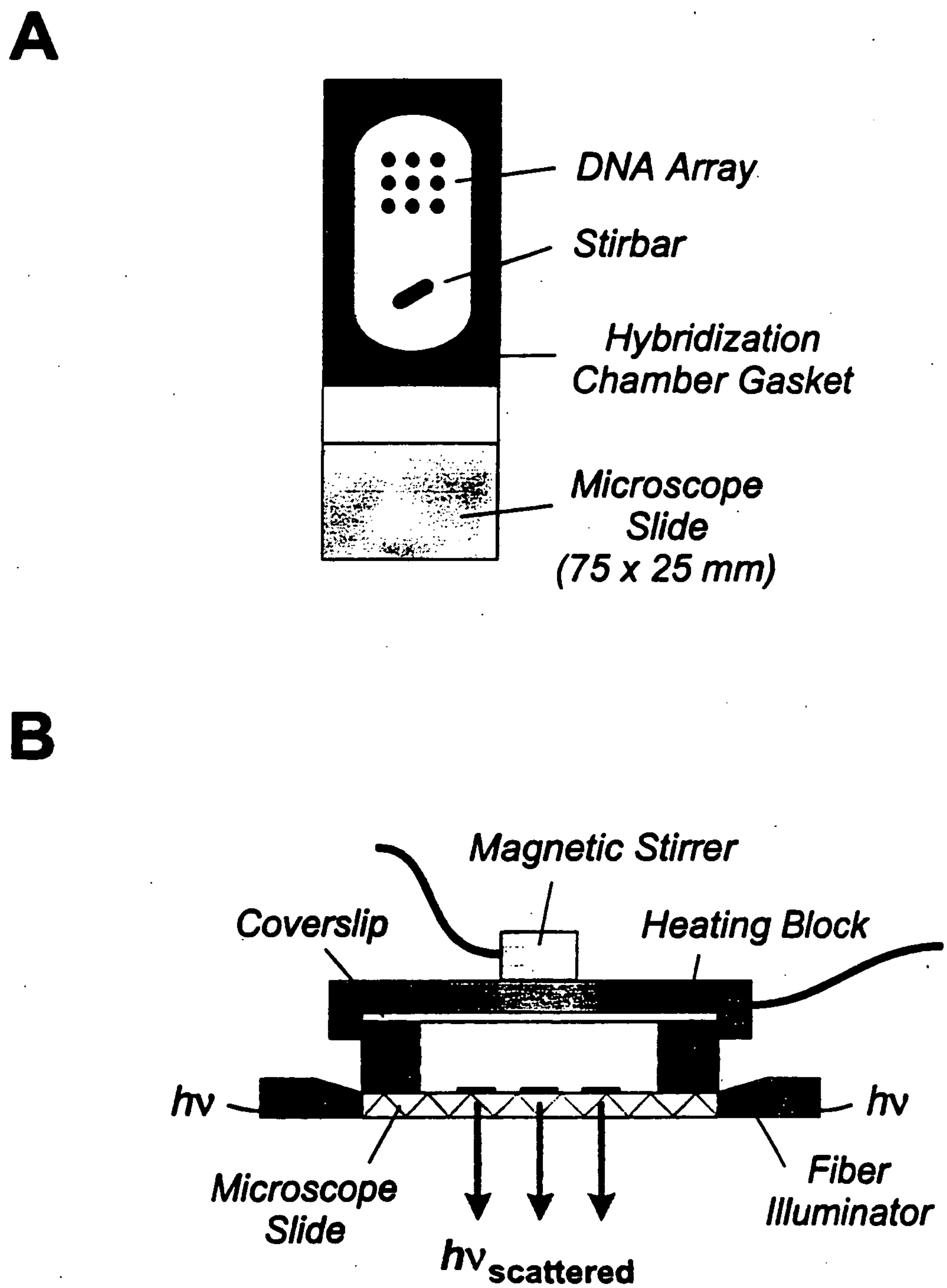


Figure 65


A
DNA Array
Stirbar
Hybridization Chamber Gasket
Microscope Slide (75 x 25 mm)
B
Magnetic Stirrer
Coverslip
Heating Block
hν
hν
Microscope Slide
Fiber Illuminator
hν scattered

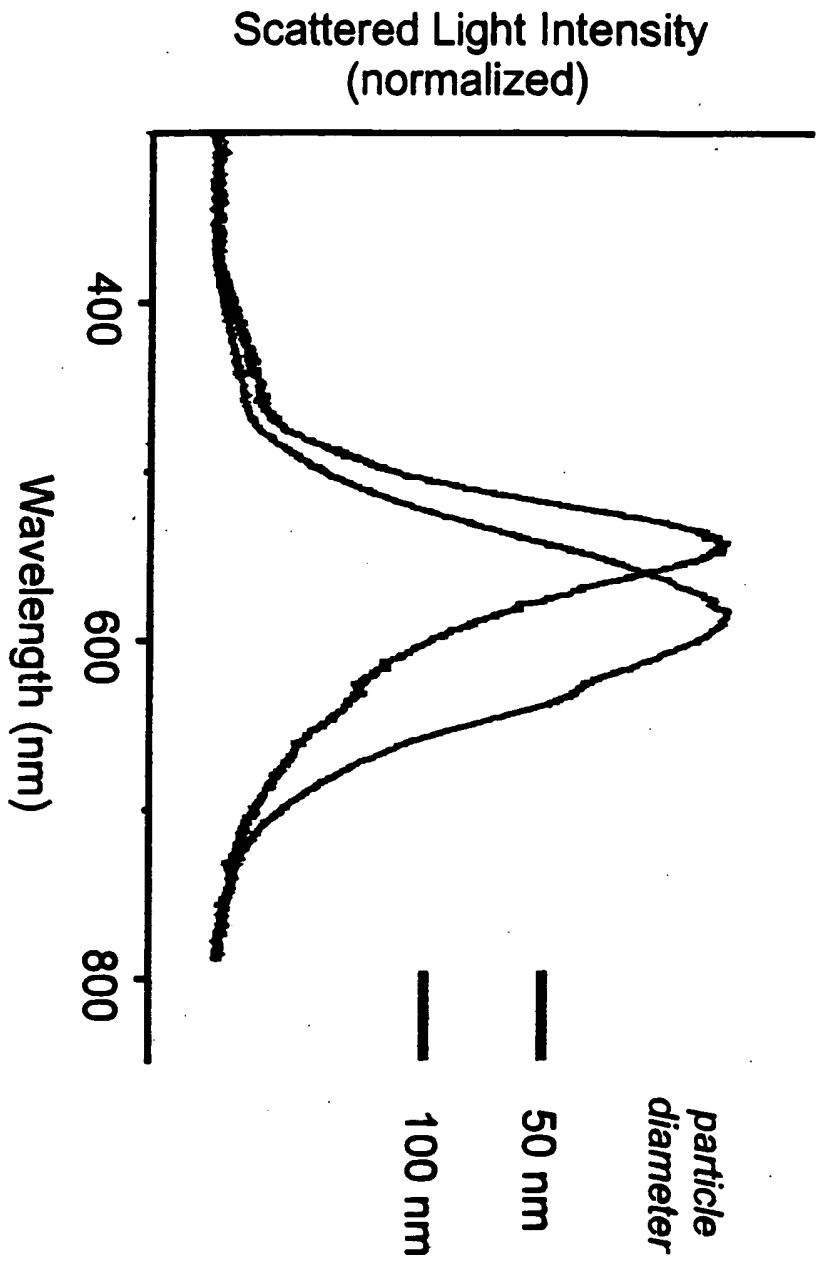


Figure 6b

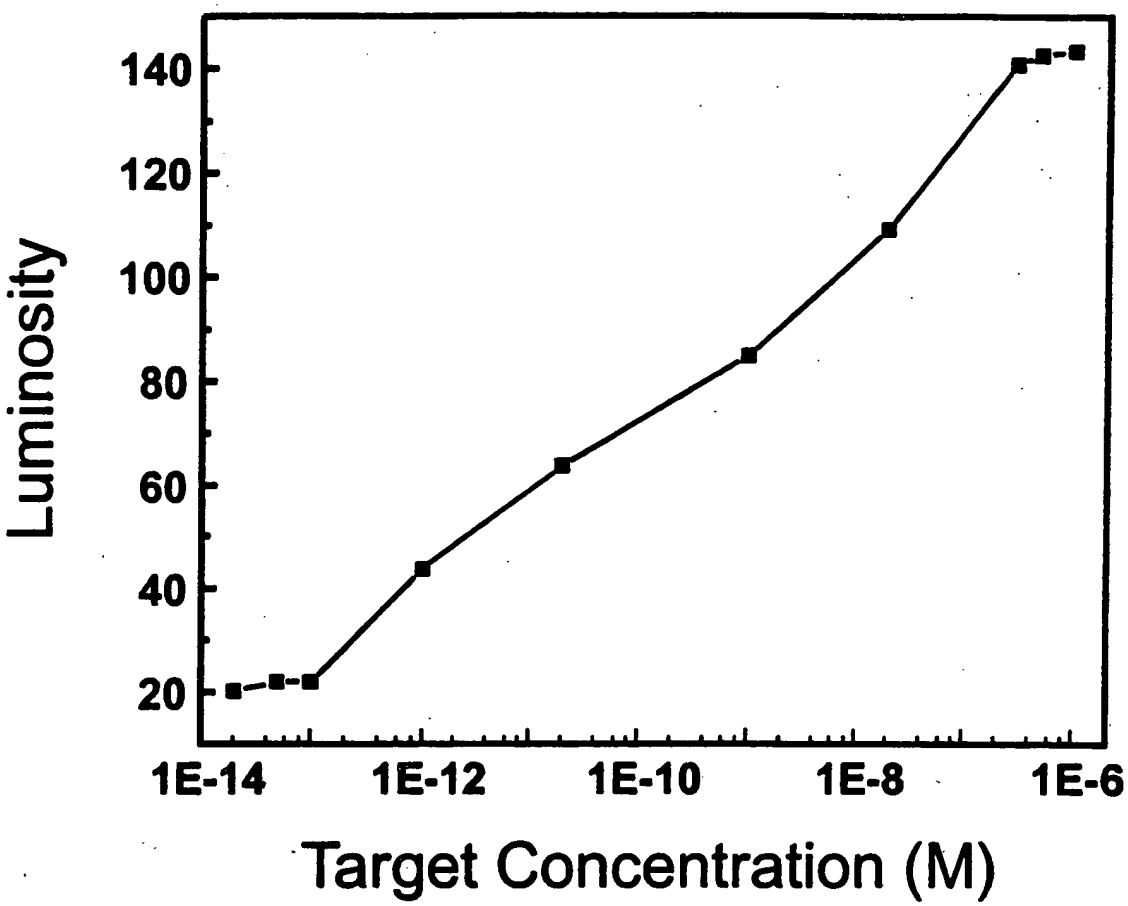

Luminosity
140
120
100
80
60
40
20
1E-14
1E-12
1E-10
1E-8
1E-6
Target Concentration (M)

Figure 67